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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS (54) Titre: PROTEINES HUMAINES A DOMAINES HYDROPHOBES ET ADN CODANT POUR CES PROTEINES (57) Abstract <p>The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.</p> (57) Abrégé <p>L'invention concerne des protéines humaines à domaines hydrophobes, des ADN codant pour ces protéines, et des vecteurs d'expression pour ces ADN, ainsi que des cellules eucaryotes exprimant ces ADN.</p>	

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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS			
(57) Abstract The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.			

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Description

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DESCRIPTION

Human Proteins Having Hydrophobic
Domains and DNAs Encoding These Proteins

TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip, so that there are

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hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is expected to lead to development of novel pharmaceuticals utilizing these proteins.

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On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto-cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

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Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,

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the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

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In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

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OBJECTS OF THE INVENTION

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The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

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BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

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Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.

Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.

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5 Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.

Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.

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10 Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.

Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.

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Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.

16 Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.

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Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.

Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.

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20 Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.

Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.

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26 Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.

Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.

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Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.

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Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

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Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10563.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01467.

Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01956.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02545.

Fig. 24 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02551.

Fig. 25 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 26 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02632.

Fig. 27 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10488.

Fig. 28 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10538.

Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10542.

Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10571.

Fig. 31 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01470.

Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02419.

Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02695.

Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10031.

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Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.

Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.

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Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.

Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10590.

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Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.

Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01462.

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Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02485.

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Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02798.

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Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10041.

Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10246.

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Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10392.

Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10489.

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Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10519.

Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10531.

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Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10574.

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SUMMARY OF THE INVENTION

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As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention. In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides DNAs coding for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

DETAILED DESCRIPTION OF THE INVENTION

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The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

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by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

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5 In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T7, T3, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

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25 In the case where one of the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region. Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system, and so on.

In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pKAl, pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells, *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium phosphate method, the liposome method, the DEAE-dextran method, and so on.

After one of the proteins of the present invention is

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expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic chromatography, affinity chromatography, reverse phase chromatography, and so on.

The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the

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scope of the present invention.

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The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method by cDNA cloning, and so on.

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The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)⁺ RNAs extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as the primers for the RT-PCR method using an mRNA isolated from human cells.

The cDNAs of the present invention are characterized by

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comprising either of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA was obtained, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

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Table 1

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SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saos-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10568	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saos-2	937	229
33, 43, 53	HP02575	Saos-2	1678	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saos-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saos-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saos-2	1753	327
64, 74, 84	HP02551	Saos-2	1117	223
65, 75, 85	HP02631	Saos-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saos-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

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91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Saos-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Saos-2	2168	487
96, 106, 116	HP10530	Saos-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02798	HT-1080	1136	267
124, 134, 144	HP10041	Saos-2	619	106
125, 135, 145	HP10246	KB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Saos-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

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Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

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In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and

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131 to 150 shall come within the scope of the present invention.

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In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

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The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

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In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

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Research Uses and Utilities

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The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

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protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

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levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be

administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular

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Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

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5 Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and
10 Measurement of mouse and human Interferon γ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

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Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without
15 limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-
20 1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6-
35 Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 -
40 Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991;
45 Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.
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6.13.1, John Wiley and Sons, Toronto. 1991.

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Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp.

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and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

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Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

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Using the proteins of the invention it may also be possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

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has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

5 Down regulating or preventing one or more antigen
functions (including without limitation B lymphocyte antigen
functions (such as , for example, B7)), e.g., preventing
high level lymphokine synthesis by activated T cells, will
be useful in situations of tissue, skin and organ
transplantation and in graft-versus-host disease (GVHD).
10 For example, blockage of T cell function should result in
reduced tissue destruction in tissue transplantation.
Typically, in tissue transplants, rejection of the
transplant is initiated through its recognition as foreign
by T cells, followed by an immune reaction that destroys the
15 transplant. The administration of a molecule which inhibits
or blocks interaction of a B7 lymphocyte antigen with its
natural ligand(s) on immune cells (such as a soluble,
monomeric form of a peptide having B7-2 activity alone or in
conjunction with a monomeric form of a peptide having an
20 activity of another B lymphocyte antigen (e.g., B7-1, B7-3)
or blocking antibody), prior to transplantation can lead to
the binding of the molecule to the natural ligand(s) on the
immune cells without transmitting the corresponding
costimulatory signal. Blocking B lymphocyte antigen
25 function in this matter prevents cytokine synthesis by
immune cells, such as T cells, and thus acts as an
immunosuppressant. Moreover, the lack of costimulation may
also be sufficient to anergize the T cells, thereby inducing
tolerance in a subject. Induction of long-term tolerance by
30 B lymphocyte antigen-blocking reagents may avoid the
necessity of repeated administration of these blocking
reagents. To achieve sufficient immunosuppression or

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tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

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The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

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Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

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autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the

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transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

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In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

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The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and , microglobulin protein or an MHC class

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II chain protein and an MHC class II chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

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The activity of a protein of the invention may, among other means, be measured by the following methods:

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Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J.

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Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

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5 Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

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15 Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

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25 Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,

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1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

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5 Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

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Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

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Hematopoiesis Regulating Activity

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A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

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stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

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Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

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Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

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A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

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A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is

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not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

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in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

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trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

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Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

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It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

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A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

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A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

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The activity of a protein of the invention may, among other means, be measured by the following methods:

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Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

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International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

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5 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

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Activin/Inhibin Activity

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A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

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The activity of a protein of the invention may, among

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other means, be measured by the following methods:

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Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

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10 A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

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25 A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

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The activity of a protein of the invention may, among

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other means, be measured by the following methods:

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Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

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A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

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The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

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without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

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Receptor/Ligand Activity

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A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

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The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

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Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987;
Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein
et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et
al., J. Immunol. Methods 175:59-68, 1994; Stitt et al.,
Cell 80:661-670, 1995.

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Anti-Inflammatory Activity

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Proteins of the present invention may also exhibit
anti-inflammatory activity. The anti-inflammatory activity
may be achieved by providing a stimulus to cells involved in
the inflammatory response, by inhibiting or promoting cell-
cell interactions (such as, for example, cell adhesion), by
inhibiting or promoting chemotaxis of cells involved in the
inflammatory process, inhibiting or promoting cell
extravasation, or by stimulating or suppressing production
of other factors which more directly inhibit or promote an
inflammatory response. Proteins exhibiting such activities
can be used to treat inflammatory conditions including
chronic or acute conditions), including without limitation
inflammation associated with infection (such as septic shock,
sepsis or systemic inflammatory response syndrome (SIRS)),
ischemia-reperfusion injury, endotoxin lethality, arthritis,
complement-mediated hyperacute rejection, nephritis,
cytokine or chemokine-induced lung injury, inflammatory
bowel disease, Crohn's disease or resulting from over
production of cytokines such as TNF or IL-1. Proteins of the
invention may also be useful to treat anaphylaxis and
hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

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In addition to the activities described above for
immunological treatment or prevention of tumors, a protein
of the invention may exhibit other anti-tumor activities. A

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protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

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embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

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Examples

The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

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(1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

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The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saos-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

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carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA libraries. Full-length cDNA clones were selected from respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

(2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a T₇ rabbit reticulocyte lysate kit (Promega). In this case, [³⁵S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25 μ l containing 12.5 μ l μ of T₇ rabbit reticulocyte lysate, 0.5 μ l of a buffer solution (attached to the kit), 2 μ l of an amino acid mixture (without methionine), 2 μ l of [³⁵S]methionine (Amersham) (0.37 MBq/ μ l), 0.5 μ l of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

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out by adding to this reaction system 2.5 μ l of a canine pancreas microsome fraction (Promega). To 3 μ l of the resulting reaction solution was added 2 μ l of the SDS sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

(3) Expression by COS7

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Escherichia coli cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100 μ g/ml of ampicillin, the helper phage M13K07 (50 μ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100 μ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

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The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO₂ in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc, well diameter: 3 cm) were inoculated with 1×10^5 COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO₂. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the resulting cells was added a suspension of 1 μ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3 μ l of

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TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO₂. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO₂. After the culture medium was replaced by a culture medium containing [³⁵S]cystine or [³⁵S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

(4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (GenBank Accession No. Z93382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

C. elegans hypothetical protein F45G2.c (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region.

Table 2

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10 HP MAKYLAQIIVMGVQVVGRAFARALRQEF-----AASRAAADARGRAGHRSAAASNLS-
    .. . *..*.*.*.*.*. **..**.....*.**.*.
CE MPWRTALKVALAAGEAVAKALTRAVRDEIKQTQQAAARHAASTGQSASETRENANSNAKL
HP GLSLQEAAQILNV-SKLSPEEVQKNYEHLFKVNDKSVGGSFYLQSKVVRAKERLDEEL-K
    ***.*. *****. *.*****.*****.*****.*****.*****.***.
15 CE GISLEESQLILNVKTPLNREEVEKHIEHLFNINDKSKGGTLYLQSKVFRAKERIDEEZGR
HP IQAQEDREKGMPHT
    *.*****.
CE IELKEEKKKEENAKTE

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA338859) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02593> (SEQ ID Nos. 2, 12, and 22)

Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA306490) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10195> (SEQ ID Nos. 3, 13, and 23)

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Determination of the whole base sequence of the cDNA insert of clone HP10195 obtained from cDNA library of human fibrosarcoma HT-1080 revealed the structure consisting of a 286-bp 5'-untranslated region, a 729-bp ORF, and a 604-bp 3'-untranslated region. The ORF codes for a protein consisting of 242 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was somewhat larger than the molecular weight of 27,300 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed the registration of sequences that were similar to the Aplysia VAP-33 (SWISS-PROT Accession No. P53173). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the Aplysia VAP-33 (AP). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the

present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 46.5% in the entire region.

Table 4

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HP MAKHEQILVLDPPDLDKPKGFFTDVVTTNLKLRNPSDRKVCFKVKTAPRRYCVRPNSGI
  *.*** *.***.***.***.***.***.***.***.***.***.***.***.***.***
AP MASHEQALILEPAGELRFKGFPTDVVTADLKLNSPTDRRICFKVKTAPKRYCVRPNSGI
HP IDPGSTVTVSVMLQFFDYDPNEKSKHKFMVQTIFFAPPNTSD-MEAVWKEAKPDELMDSKL
  ..* .....***.***.***.***.***.***.***.***.***.***.***.***
AP LEPKTSIAVAVMLQFFNYDPNEKNKHKFMVQSMYAPDHVVESQELLWKDAPPESLMDTKL
HP RCVFEMPENNDKLNDEPSK-----AVPLNASKQDGPMPKP-HSVSLNDTE
  *****.....*.***.***.***.***.***.***.***.***.***.***.***
AP RCVFEMPDGSHQAPASDASRATDAGAHFSZSALEDPTVASRKTETQSPKRVGAVGSAGED
HP TRKLMECKRLQGEMMKLSEENRHLRDEGLRLRKVAHSD--KPGSTSTASFRDNVTSPLP
  ..**.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*.*
AP VKKLQHELKKAQSEITSLKGENSEQLKDEGIRLRKVAMTDTVSPTPLNPSAPAAAVRAFP
HP SLLVVIAAIFIGFPLGKFI
  ...*.***.***.***.***.***.***.***.***.***.***.***.***
AP PVVYVVAAILGLIIGKPLL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA447905) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10423> (SEQ ID Nos. 4, 14, and 24)

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Determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

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Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10507> (SEQ ID Nos. 6, 16, and 26)

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Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

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are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

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Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10566> (SEQ ID Nos. 8, 18, and 28)

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Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,452 predicted from the ORF. When expressed in COS7 cells, an expression product of about 12 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W79821) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10567> (SEQ ID Nos. 9, 19, and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10567 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 77-bp 5'-untranslated region, a 375-bp ORF, and a 133-bp 3'-untranslated region. The ORF codes for a protein consisting of 124 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 14,484 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA428475) in ESTs, but, since they

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are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

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Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen

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(SWISS-PROT Accession No. Q99795). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human cell-surface A33 antigen (A3). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.0% in the N-terminal region of 243 residues.

Table 5

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HP	MAELPGPFLCGALLGFLCLSGLA	VEVKVPT	ETPLSTPLGKTAELTCTYSTSV	GD	SFAL-EW
			*....	**.....**
A3	MVGKMWPVLWTLCAVRVTVD	DAISVETPQD	VLRSQGKSVTL	PCTYHTSTSS	REGLIQW
HP	SFVQPGKPISESHPI	LYFTNGHLYPTG	SKSRVSL	LQNPPTVG	VATLKLTDVHPSDTGT
	* * . * .	*	*.....*
A3	DKLL--LTH	TERVVVWPF	SNKN-YIH	GELYKNRVS	ISNNAEQSDASITIDQLIMADNGTY
HP	LCQVNNPPDFY	TNGLGLINLT	VLVPPSNPL	CSQSGQTSV	GGSTALRCSSSEGAPKPVYNW
	* * .	* .	* .	* .	* .
A3	ECSVSLMSD	LEGNTKSRV	RLVLP	PSKPEC	GIEGETIIGNNIQLTCQSK
HP	VR	LGTFFTPSP	GS	MSVQDEV	SGQLILTNLSLTSSGTYRCVATNQMG
	*	*	*	*	*
A3	KRYN	ILNQEQP--	LAQPASG	QPVSLKN	ISTDTSGYICTSSNEEGTQFCNITVA
HP	-QGRV	AGALIGVLL	GVLLS	VAAFLV	RFQKERGKKPKETYGGSDLREDALAPGISEHTC
	. . *	* .	* .	* .	* .
A3	NVALYV	GIAVG	VVAALII	IGII	YCCCRGKDDNTEDKEDARPNREAYE
HP	MRADSS	KGFLERP	SSASTV	TTKSK	LP
A3	EREEED	YRQZE	QRSTGR	ESPD	HLDQ

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

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of sequences that shared a homology of 90% or more (for example, Accession No. T24595) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP01426> (SEQ ID Nos. 31, 41, and 51)

Determination of the whole base sequence of the cDNA insert of clone HP01426 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 1-bp 5'-untranslated region, a 942-bp ORF, and a 122-bp 3'-untranslated region. The ORF codes for a protein consisting of 313 amino acid residues and there existed a putative secretory signal. Figure 11 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 34,955 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 38 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ser-Ser at position 163). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from tryptophan at position 17. When expressed in COS7 cells, an expression product of about 39 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the

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protein was similar to the *Xenopus laevis* cortical granule lectin (EMBL Accession No. X82626). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *X. laevis* cortical granule lectin (XL). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the region other than the N-terminal region.

Table 6

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HP MNQLSFLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRT
  *   **               *           *****. . * * * * .
XL MLVHILLLLVTGGLSQSCEPVVIVASKNMVKQLDCDKFRSCKEIKDSNEEAQDGIYTLTS
HP ENGVIIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANY
  ..* .*****.*****.* ****.*****.*****
XL SDGISYQTFCDMTTNGGGWTLVASVHENNMAGKCTIGDRWSSQQGNRADYPEGDGNWANY
HP NTFGSAAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLG
  *****.*****.* .**.******. ***** * * * . *
XL NTFGSAGGATSDDYKNPGYYDIEAYNLGVWHVPNKTPLSVWRNSSLQRYRTTDGILFKHG
HP HNLPGIYQKYPVKYGECKCWTDNQGPVIVVYDFGDAQKTASYSPYQGREFTAGFVQFRV
  ***..* .***** * .* .**.******.*. ***.*** ..*.*.*
XL GNLFSLYRIYPVKYIGIGSCSKDSGPTVPVVYDLGSARKLTASFYSPDFRSQFTPGYIQFRP
HP FNNERAANALCAGMRVTGCNTEHHCIGGGGYFPEASPQQCGDFSGFDWSGYGVYSSS
  ..*.* * * * .**.*.*.*****.*.*****.***** *..
XL INTEKAALALCPGMKMSCNVHVCIGGGGYFPEADPRQCGDFAAYDFNGYGTKKFNSAG
HP REITEAAVLLFYR
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XL IEITEAAVLLPYL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R06009) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02515> (SEQ ID Nos. 32, 42, and 52)

Determination of the whole base sequence of the cDNA insert of clone HP02515 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 176-bp 5'-untranslated region, a 690-bp ORF, and a 71-bp 3'-untranslated region. The ORF codes for a protein consisting of 229 amino acid residues and there existed a putative secretory signal at N-terminus and one putative transmembrane domain at the C-terminus. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was almost identical with the molecular weight of 26,000 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 25.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from phenylalanine at position 28.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human T1/ST2 receptor binding protein (GenBank Accession No. U41804). Table 7 shows the

comparison between amino acid sequences of the human protein of the present invention (HP) and the human T1/ST2 receptor binding protein (T1). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 55.8% in the entire region.

Table 7

HP	MGDKIWLPPFPVLLLAALFPVLLPGAAGFTPSLDSDFTFLLPAGQKECFYQPMPLKASLE
	*.... ** .*** . *** . * *
T1	MMAAGAALALALWLL--MPPFEV-GGAGPPPIQDGEFTFLPAGRKQCFYQSAPANASLE
HP	IEYQVLDGAGLDIDFHLASPEGKTLVFEQRKSDGVHTVE-TEVGDMFCPDNTFTSTISER
* * * * *
T1	TEYQVIGGAGLDVDFTLSPQGVLLVSESRRKADGVHTVEPTACDYKLCFDSNFSFTISER
HP	VIFFELILDNMGEQAQEQEDWKYITGTDILDMKLEDILESINSIKSRLSKSGHIQILLR
* * * * *
T1	LVFFELIFDSL-QDDEEVEGWAEAVEPEEMLDVKMEDIKESIETMRRLERSIQMLTLRL
HP	APEARDRNIQESNFDVNFWSMVNLVVMVVSAIQVYMLKSLFEDKRKRSRT
* * * * *
T1	APEARDRNLQEGNLERVNFWSAVNVAVLLLVAVLQVCTLKRPFQDKRPVPT

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA381943) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP02575> (SEQ ID Nos. 33, 43, and 53)

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Determination of the whole base sequence of the cDNA insert of clone HP02575 obtained from cDNA library of human osteosarcome cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1404-bp ORF, and a 219-bp 3'-untranslated region. The ORF codes for a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 13 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was almost identical with the molecular weight of 54,065 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 57 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exist in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Arg-Thr at position 171, Asn-Ser-Thr at position 239 and Asn-Asp-Thr at position 377). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 29. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the supernatant fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human α -L-fucosidase (SWISS-PROT Accession No. P04066). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human α -L-fucosidase (FC). Therein,

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the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both

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Table 8

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HP MRPQELPRLAPLLLLLLLLLPPPPC-PAHSATRFDPWTWESLDARQLPAWFDQAKFGIFI
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC MRSRPAGPALLLLLLFLGAESVRRSQPPRRYTPDWPSLDSRPLPAWFEAKFGVPI
HP HWGVFSVPSFGSEFWWWYQKEKIPKYVEFMKDNYPSPFKYEDFGPLFTAKFFNANQWAD
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC HWGVFSVPAWGSEFWWWHQGEGRPQYQRFMRDNYPGFSYADFGPQFTARFFHPEEWAD
HP IFQASGAKYIVLTSKHHEGFTLWGSEYSWNWNAIDEGPKRDIVKELEVAIRNRDRLRFGI
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC LFQAAGAKYVVLTTKHHEGFTNWPSVSWNWSKDVGPHRDLVGELGTALRKR-NIRYGL
HP YYSLEWFHPLFLEDESSFHKKRQFPVSKTLPELYELVNNYQPEVLWSDGDCGAPDQYWN
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC YHSLEWFHPLYLLDKKNGFKTQHFVSARTMPELYDLVNSYKPDLIWSDGEWECPDITYN
HP STGFLAWLYNESPVRGTVVINDRWGAGSICKHGGFYTCSDRYNPGHLLPHKWENCMITDK
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC STNFLSWLYNDSPVKDEVVNDRWGQNCSCHEGGYNCBDFKPKQSLPDHKWEMCTSIDK
HP LSWGYRREAGISDYLTIEELVKQLVETVSCGNLLMNIGPTLDGTISVVFEEERLRQMGSW
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC FSWGYRRDMALSDVTEESEIISLVQTVSLGNYLLNIGPTKDGLVPIFQERLLAVGKW
HP LKVNGEAIYETHWRSQNDTVTPDVWYTSKPKEKLVYAIFLKWFTSGQLFGLHFKAILGA
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC LSINGEAIYASKPWRVQWEKNTTSVWYTSKGSA--VYAIFLHWPENGVLNLESPITT-ST
HP TEVKLLGHGQPLNWLISLEQNGIMVELPQLTIHQMPCKKWCWALALTNI
      ***** * . . . . . * . . . . * . . . . * . . . . * . . . . *
FC TKITMLGIQGLKWSTDPDKGLFISLPQLPPSAVPAEPANTIKLTGVR

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N28668) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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10 <HP10357> (SEQ ID Nos. 34, 44, and 54)

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Determination of the whole base sequence of the cDNA insert of clone HP10357 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 113-bp 5'-untranslated region, a 300-bp ORF, and a 54-bp 3'-untranslated region. The ORF codes for a protein consisting of 99 amino acid residues and there existed two putative transmembrane domains. Figure 14 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 11 kDa that was almost identical with the molecular weight of 10,923 predicted from the ORF.

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25 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA477156) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10447> (SEQ ID Nos. 35, 45, and 55)

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Determination of the whole base sequence of the cDNA

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insert of clone HP10447 obtained from cDNA library of human liver revealed the structure consisting of a 271-bp 5'-untranslated region, a 570-bp ORF, and a 34-bp 3'-untranslated region. The ORF codes for a protein consisting of 189 amino acid residues and there existed five putative transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA296976) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10477> (SEQ ID Nos. 36, 46, and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10477 obtained from cDNA library of human liver revealed the structure consisting of a 149-bp 5'-untranslated region, a 1092-bp ORF, and a 15-bp 3'-untranslated region. The ORF codes for a protein consisting of 363 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,884 predicted from the ORF.

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The search of the protein data base using the amino

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

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of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10513> (SEQ ID Nos. 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10513 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 134-bp 5'-untranslated region, a 750-bp ORF, and a 0-bp 3'-untranslated region. The ORF codes for a protein consisting of 249 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 27,373 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0512 (GenBank Accession No. AB011084). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0512 (KI). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 31.6% in the C-terminal region of 196 amino acid residues.

Table 10

5	5	HP	MGGPRGAGWVAAGLLLGAGACYCIYRLTRGRRRG
15		KI	RGRGRRPVAMQKRPFYIDEILGVRDLRKVLALLQKSDDPFIQQVALLTSLNNANYSCN
		HP	DRELGIRSSKSAEDLTDGSYDDVLNAEQQLKLLYLESTEDPVIIERALITLGNNAAFSV
			** . * *. *.. *
20		KI	QETIRKLGGLPIIANMINKTDPHIKEKALMAMNNLSENTEYQGRQLQVYMNKVMDDIMASN
	10	HP	NQAIIRELGGIPIVANKINHSNQSISKEKALNALNNLSVNVENQIKIKVQVLKLLNLSEN
		 * .. . *... * ****..**.* ..**
		KI	LNSAVQVVGLKFLTNMTITNDYQHLLVNSIANF--FRLSQGGGKIKVEILKILSNFAEN
25		HP	PAMTEGLLRAQVDSFSLSYDSHVAKIILLRVLTLPQNIKNCLKIEGHLAVQPTFTTGSLS
			. . **..** . ** **..*..**..**..**..* . * . * **
	15	KI	PDMLKLLSTQVPASFSSLYNSYVESEILINALTLFEIYDNLRAE--VFNYREFNKGSL
		HP	FPL-LHGECAQKIRALVDHHDABVKEKVVTIIPKI
			. .. *..*****..** ** **..*..* .
30		KI	FYLCCTSGVCVKKIRALANHHDLLVKVKVIKLVNKF

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N92228) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10540> (SEQ ID Nos. 38, 48, and 58)

Determination of the whole base sequence of the cDNA insert of clone HP10540 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure

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consisting of a 47-bp 5'-untranslated region, a 297-bp ORF, and a 245-bp 3'-untranslated region. The ORF codes for a protein consisting of 98 amino acid residues and there existed two putative transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CEF49C12.12 (GenBank Accession No. Z68227). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CEF49C12.12 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.1% in the entire region.

Table 11

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25	HP M-ASLLCCGPRLAACGIVLSAWGVIMLIMLGIPFNVHSAVLIEDVPFTEKDPENGPNQNIY
	* *** * * * * * * * * * * * * *
	CE MGKICPLMGPRMSAPCMVMSVGVIFLGLLGVPFYIQAVTLFPDLHF-EGHGKVPSSVID
45	HP NLYEQVSYNCFIAAGLYLLGGFSFCQVRLNKRKEYMVR
	* * * * * * * * * *
30	CE AKYNEKATQCWIAAGLYAVTLIAVFWQ---NKYNTAQIF

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA420715) in ESTs; but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

10 <HP10557> (SEQ ID Nos. 39, 49, and 59)

Determination of the whole base sequence of the cDNA insert of clone HP10557 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 24-bp 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-untranslated region. The ORF codes for a protein consisting of 172 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was larger than the molecular weight of 18,844 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 39 kDa which is considered to have been subjected to some modification after secretion. In addition, there exist in the amino acid sequence of this protein no site at which N-glycosylation may occur. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 32. When expressed in COS7 cells, an expression product of about 20 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human progesterone binding protein (EMBL Accession No. AJ002030). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human progesterone binding protein (PG). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.5% in the C-terminal region of 151 amino acid residues.

Table 12

HP	MVGPAP
PG MAAGDGDVKGTLGSGSESSNDGGSESPGDAGAAAEAGGWAALALLTGGEMLLNVAL	
HP RRRRLRPLAALALVLALAPGLPTARAGQTPRPAERGPPV--RLFTEEELARYGGEEDQPI	
PG VALVLLGAYRLWVRWGRRGLGAGAGAGEESPATSLPRMKRDFSLEQLRQYDG--SRNPRI	
HP YLAVKGVVFDVTSGREFYGRGAPYNALTGKDSTRGVAKMSLDPADLTHDTHGLTAKELEA	
PG LLAVNGKVFDVTKGSKFYGPAGPYGIFAGRDASRGLATFCLDKDALRDEYDDLSDLNVAQ	
HP LDEV--FTKVYKAKYPIVGYTARRILNEDGSPNLDKPEDQPHFDIKDEF	
PG MESVREWEMQFKEY---DYVG-RLKPGGEPS-EYTDEEDTKDHNKQD	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AAL01709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10563> (SEQ ID Nos. 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (GenBank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A. thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.5% in the entire region.

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Table 14

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acid sequence of the present protein revealed that the protein was similar to the rat Sec22 homologue (GenBank Accession No. U42209). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat Sec22 homologue (RN). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 94.6% in the N-terminal region of 241 amino acid residues. The protein of the present invention was longer by 53 amino acids at the C-terminus than the rat Sec22 homologue.

HP	MSMILSASVIRVRDGLPLSASTDYEQSTGMQECRKYFKMLSRKLAQLPDRCTLKTGHYNI
	*****.*****.***.*.*****.*****..**
RN	MSMILSASVVRVRDGLPLSASTDCEQSAGVQECRKYFKMLSRKLAQFPDRCTLKTGRHNI
HP	NFISSLGVS YMMLCTENYPNVLA FSFLDELQKEFITT YNMMKTNTAVR PYCFIEFDNFIQ

RN	NFISSLGVS YMMLCTENYPNVLA FSFLDELQKEFITT YNMMKTNTAVR PYCFIEFDNFIQ
HP	RTKQRYNNPRSLSTKINLSDMQTEIKLRPPYQISMCELG SANGVTSAPSVDC KGAGKISS
	*****.*****.*****
RN	RTKQRYNNPRSLSTKINLSDMQMEIKLRPPYQIPMCELG SANGVTSAPSVDC KGAGKISS
HP	AHQRLPATLSGIVGFILSL LCGALNLIRGFHAIESLLQSDGDDFN YIIAFLGTAACLY
	*****.*****.***.*.*****
RN	AHQRLPATLSGIVAFILSL LCGALNLIRGFHAIESLLQSDGEDFS YMIAFLGTAACLY
HP	QCYLLVYYTGWRNVKSFLT FGLICLCNMYLYELRN LWQLFFHVTVGAFVTLQIWLROAQG
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RN	QMICLCLQGRKERT

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA421925) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP01956> (SEQ ID Nos. 62, 72, and 82)

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Determination of the whole base sequence of the cDNA insert of clone HP01956 obtained from cDNA library of human liver revealed the structure consisting of a 86-bp 5'-untranslated region, a 552-bp ORF, and a 359-bp 3'-untranslated region. The ORF codes for a protein consisting of 183 amino acid residues and there existed one putative transmembrane domain. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20.5 kDa that was almost identical with the molecular weight of 20,073 predicted from the ORF.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the yeast hypothetical protein 21.5 kDa (SWISS-PROT Accession No. P53073). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the yeast hypothetical protein 21.5 kDa (SC). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

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of 34.3% in the C-terminal region of 108 amino acid residues.

Table 15

5	HP	MTAQGGGLVANRGRFRKWAIELSGPGGSGRGRSDRGSGQGDSLYPVGYLDKQVPDTS
10	SC	MSEQEPYEWAKHLLDTKYIEKYNIQNSNTLPSPGPEGNSSKGNVTRKQDQDTSQTSLA
15	HP	VQETDRILVEKRCWDIALGPLKQIPMNLFIMYMAGNTISIFPTMMVCMMAWRPIQALMAI
20	10	SC QKNQITVLQVQKAWQIALQPAKSIPMNIFMSYMSGTSLQIIPINTALMLLSGPIKAIFST
25	HP	SATFK--MLESSSQKELQGLVYLIGNLMGLALAV-Y-KCQSMGLLPTHASDWLAFIEPPE
30	15	SC RSAFKPVLGNKATQSQVQTAMPFYIVFQGVLMYIGYRKLNSMGLIPNAKGDWLPWERIAH
35	HP	RMEFSGGGGLLL
40	25	SC YNNGLQWFSD

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA159753) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02545> (SEQ ID Nos. 63, 73, and 83)

Determination of the whole base sequence of the cDNA insert of clone HP02545 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 133-bp 5'-untranslated region, a 984-bp ORF, and a 636-bp 3'-untranslated region. The ORF codes for a

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protein consisting of 327 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat embigin (EMBL Accession No. AJ009698). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat embigin (RN). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 65.4% in the entire region.

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osteosarcoma cell line Saos-2 revealed the structure consisting of a 61-bp 5'-untranslated region, a 672-bp ORF, and a 384-bp 3'-untranslated region. The ORF codes for a protein consisting of 223 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was somewhat larger than the molecular weight of 24,555 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 26 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 20.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse FGF binding protein (GenBank Accession No. U49641). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse FGF binding protein (MM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 21.2% in the entire region other than the N-terminal region. In particular, all the eight cysteine residues contained in the both proteins were conserved.

Table 17

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HP                               MKFVPCLLLVTLSCGLTLGQAPRQKQGST
                                ...*...
5 MM MRLHSLILLSFLLLATQAFSEKVRKRAKNAPHSTAEEGVEGSAPSLGKAQNKQRSRTSKS
HP GEEFHFQGTGGRDSCMRPSSLGQAGVWLRVDCRNTDQTYWCEYRGQPSMCQAFADPK
  ..*...
MM LTHGKFVTKDQATC---RWAVTEEEQGISLKVQCTQADQEFSCVFAGDPTDCLKHDKD-Q
HP SYWNQALQELRLHACQGA-PVLRPSVCREAGPQAHMQQVTSSLKGSPEPNQQPEAGTP
10 **...
MM IYWKQVARTLRKQKNICRDAKSVLKTRVCRKRFEPESNLKLVNPNARGNTKPRKEAEVSA
HP SLRPKATVKLTATQLGKDSMEELGKAKPTTRPTAKPTQPGPRPGNEEAKKAWHCWK
  ..*...
25 MM REHNKVQEAVSTEPNRIKEDI-TLNPAATQTM-TIRDPECLEDDPVLNQ-RKTALEFCGE
15 HP PFQALCAFLISFFRG
  ..*...
MM SWSSICTFFLNMLQATSC

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA317400) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02631> (SEQ ID Nos. 65, 75, and 85)

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,

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and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N50907) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10488> (SEQ ID Nos. 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10488 obtained from cDNA library of human liver revealed the structure consisting of a 39-bp 5'-untranslated region, a 273-bp ORF, and a 421-bp 3'-untranslated region. The ORF codes for a protein consisting of 90 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,151 predicted from the ORF. When expressed in COS7 cells, an expression product of about 6 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H73534) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10538> (SEQ ID Nos. 68, 78, and 88)

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Determination of the whole base sequence of the cDNA insert of clone HP10538 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 357-bp 5'-untranslated region, a 1500-bp ORF, and a 1911-bp 3'-untranslated region. The ORF codes for a protein consisting of 499 amino acid residues and there existed at least four putative transmembrane domains. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse pore-forming K⁺ channel subunit (GenBank Accession No. AF056492). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse pore-forming K⁺ channel subunit (MM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 32.4% in the N-terminal region of 241 amino acid residues.

Table 19

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HP  MVDRCPLLTSIAIFYLAIGAAIFEVLEEPHWKEAKKNYYTQRLLELLKEFPCLGQEGLDK
      * . . . . . * * . . . . . * * . . . . . * * . . . . . * * . . . . .
5  MM MRSTLLALLLVLLYLVS GALVFQALEQPHEQQAQKKMDHGRDQFLRDHPCVSQKSLED
HP  ILEVVS DAAGQG-----VAITGNQTFNNWNWPNAMIFRAATVITTIGYGNVAPKTPAGRLF
      . . . . . * * * . . . . . * * . . . . . * * . . . . . * * . . . . .
MM  FIKLLVEALGGGANPETSWTNSSNHSSANWLGSAFFFSGTIIITTIGYGNIVLHETDAGRLF
HP  CVFYGLFGVPLCLTWISALGKFFGGRAKR----LGQPLTKRGVSLRKAQITCTVIFIVWG
10 * . . . . . * * * . . . . . * * . . . . . * * . . . . . * * . . . . .
MM  CIFYALVGIPFLFGMLLAGVGDRLGSSLRRGIGHIEAIFLKWHPGLVRSLSAVLELLIG
HP  VLVHLVIPPFVFMVTEGWNIEGLYYSPITISTIGFGDFVAGVNPSSANYHALYRYPVELW
      * . . . . . * * . . . . . * * . . . . . * * . . . . . * * . . . . .
25 MM  CLLFVLTPTFVFSYMSWSKLEAIYFVIVTLTTVGFGDYVPG--DGTGQNSPAYQPLVWFW
15 HP  IYLGlawLSLFVNWKVSMPFEVHKAIKRRRRRRKESFESSPHSRKALQVKGSTASKDVNI
      * . . . . .
MM  ILFGLAYFASVLTITIGNWLRVSRRTAEMGGLTAQAASWTGTVTARVTQRTGFSAPFFE

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R25184) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10542> (SEQ ID Nos. 69, 79, and 89)

Determination of the whole base sequence of the cDNA insert of clone HP10542 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 23-bp 5'-untranslated region, a 321-bp ORF, and a 426-bp 3'-

untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,724 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA029683) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10571> (SEQ ID Nos. 70, 80, and 90)

Determination of the whole base sequence of the cDNA insert of clone HP10571 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 95-bp 5'-untranslated region, a 459-bp ORF, and a 675-bp 3'-untranslated region. The ORF codes for a protein consisting of 152 amino acid residues and there existed one putative transmembrane domain. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20 kDa that was larger than the molecular weight of 17,062 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 23 kDa

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which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ile-Thr at position 10).

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5 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA105822) in ESTs, but, since they are partial sequences, it can not be judged whether or not 10 any of these sequences codes for the same protein as the protein of the present invention.

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<HP01470> (SEQ ID Nos. 91, 101, and 111)

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Determination of the whole base sequence of the cDNA insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight of 40,489 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to have been subjected to some modification. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 23. When

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expressed in COS7 cells, an expression product of about 44 kDa was observed in the supernatant fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein 39.9 kDa (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 58.9% in the entire region.

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Table 20

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HP MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRASIKDIKKAYRKALQLHPDRNPDD
      *.. * *****...* ..***** ..*****..*
5 CE MRILNVSLVLAASSLVAFVECGRDFYKILGVAKNANANQIKKAYRKALQELHPDRNQDD
HP PQAQEKFDLGAAYEVLSDSEKQYDTYGEGL--KDGHQSSHGDIFSHFFGDFGFMFG
      *..*****..*****..* * ..* * ..* * ..* * ..* * ..* * ..*
10 CE EMANEKFQDLSSAYEVLSDKEKRAMYDRHGEEGVAKMGGGGGGGHDPFSSFFGDF-FG-G
HP GTPRQQRNIPRGSDIIVDLVTLLEVYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTT
      *..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*
15 CE GGGHGGEGTTPKGADVTIDLFVTLEEVYNGHFVEIKRKKAVYKQTSGRQCNCRHEMRTE
HP QLGPRGFQMTQEVVCECPNVKLVNEERTLEVEIEPGVRDGMETPFGEPEPHVDGEPGD
      *..***** * ..*****..*..*..*..*..*..*..*..*..*..*..*..*
20 CE QMGQGRFQMFQVKVCECPNVKLVQENKVEVEVEVGADNGHQQIFHGEPEPHIEGDPGD
HP LRFRIKVVKHPIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVVHISRDKITRPGAK
      *..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*
25 CE LKFKIRIQKHPFRERKGGDDLYTNVTISLQDALNGFEMEIQHLOGHIVKVRDKVTWPGAR
HP LWKKGEGLPNFDNNIKGSLIITFDVDFPKEQLTEEAREGIKQLLKQGSVQ-KVYNGLQG
      *..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*..*
30 CE LRKKDEGMPSLEDNNKGMVVTDFDVEFPKTELSDEQKAIIEILQQTIVKPRAYNGL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282838) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30 <HP002419> (SEQ ID Nos. 92, 102, and 112)

Determination of the whole base sequence of the cDNA insert of clone HP02419 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 253-bp

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5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-
untranslated region. The ORF codes for a protein consisting
of 226 amino acid residues and there existed four putative
transmembrane domains. Figure 32 depicts the
hydrophobicity/hydrophilicity profile, obtained by the Kyte-
Doolittle method, of the present protein. In vitro
translation resulted in formation of a translation product
of high molecular weight.

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The search of the protein data base using the amino
acid sequence of the present protein revealed that the
protein was similar to the human hypothetical protein
KIAA0108 (SWISS-PROT Accession No. Q15012). Table 21 shows
the comparison between amino acid sequences of the human
protein of the present invention (HP) and the human
hypothetical protein KIAA0108 (KI). Therein, the marks of -,
*, and . represent a gap, an amino acid residue identical
with that of the protein of the present invention, and an
amino acid residue similar to that of the protein of the
present invention, respectively. The both proteins shared a
homology of 43.9% in the entire region.

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of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 58 kDa. In this case, the addition of a microsome led to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL Accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the N-terminal region. Cystein was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

Table 22

HP	MRLLLL
5 CE MRIHDELQKQDMSRFGVFIIGVLPFMSVCDVLRTEEHSNHNHVEKDDFEAFGDETD HP LLVAASAMVRSEASANLGGVPSKRLKMQYATGPLLKFKICVSUCYRRVPFEYMRVISQRY	* *.. *** **...*... ..*
CE QSPSQGTEEDHIEVREQSSPVKPTAVHHAKDLPTLRIPYCVSCGYKQAFDQPTTFAKEY HP PDIRIEGENYLPQPIYRHIASFLSVFKLVLIIGLIIVGKDPFAFFGMQAPSIWQWGQENKV	*...***.*. * ..* ** *... *.. * .**.*. * * * ..**.
10 CE PNMPIEGANFAPVLWKAYVAQALSFVKMAVLVLVGGINPFERFGLGYPQILQHAGNKM HP YACMMVFFLSNMIENQCMSTGAFEITLNDVPVWSKLESGHLPMSQQLVQILDNEMKLNH	.***.*.*...*. *****. *.. ..***.*...* *...*...*
15 CE SSCMLVFMLGNLVEQSLISTGAPEVYLCNEQIWSKIESGRVPSPQEFMQLIDAQLAVLGK HP MDSIPHERS	
CE APVNTESFGEPQQTV	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02695> (SEQ ID Nos. 94, 104, and 114)

Determination of the whole base sequence of the cDNA insert of clone HP02695 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 112-bp 5'-untranslated region, a 1020-bp ORF, and a 160-bp 3'-

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untranslated region. The ORF codes for a protein consisting of 339 amino acid residues and there existed three putative transmembrane domains. Figure 34 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 38 kDa that was almost identical with the molecular weight of 38,274 kDa predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat hypertension-induced protein S-2 fragment (PIR Accession No. 539959). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat hypertension-induced protein S-2 fragment (RN). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.3% in the entire region.

Table 23

HP MNWELLWLLVLCALLLLVQLLRFLRADGDLTLLWAEWQGRPEWELTDMVWVTGASS

5 HP GIGEELAYQLSKLGVSLVLSARRVHELERVKRRCLENGNLKEKDILVLPDLTDTGSHEA
 ****.*****.***.

RN VKRRSLENGNLKEKDILVLPDLADTSSHDI

HP ATKAVLQEFGRIDILVNNGGMSQRLCMOTSLDVYRKLIENLYLGTVSLTKCVLPHMIER
 .**... ** .*.***.*****.***.

10 RN ATKTVLQEFGRIDILVNNGGVAHASLVENTNMDIPKVLIEVNYLGTVSLTKCFLPHMMER

HP KQGKIVTVNSILGIISVPLSIGYCASKHALRGFFNGLRTELATYPGIIVSNICPGPVQSN
 .*****.*

RN NQGKIVVMKS

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T84331) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10031> (SEQ ID Nos. 95, 105, and 115)

Determination of the whole base sequence of the cDNA insert of clone HP10031 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1464-bp ORF, and a 649-bp 3'-untranslated region. The ORF codes for a protein consisting of 487 amino acid residues and there existed eleven putative transmembrane domains. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained

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by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELK07H8 (GenBank Accession No. AF047659). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CELK07H8 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.2% in the entire region.

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Table 24

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HP	MDGTETRQRRLDSCGKPGELGLPHPLSTGGLPVAS
5	CE MKGGGGIGDGKKDYQSAVHEGLTTFDQLGIALEDVGKSMDAETATPGGSLFSRVIFRFRN HP EDGALRAPESQSVTPKPLETEPSRETAWSIGLQVTPFMPAGLGLSWAGMLLDYFQHWPV *...*... . . . *... . ** ** ****. .*. . . **.
10	CE ENSSLKSRTYDHSNDLVNMSVIPAESYVLFPPQVLPFFAVAGLGMVFAGLVLSIVVTWPL HP FVEVKDLLTLVPPLVGLKGNLEMTLASRLSTAANTGQIDDPQEQHRVISSNLALIQQAT * * . .*.***.*.***** ** *... . . . * . ****.*****
15	CE FEEIPEILILVPALLGLKGNLEMTLASRLSTLANLGHMDSSKQRKDVVIANLALVQVQAT HP VVGLAABAALLGVVSREEVDVAKVELLCASSVLTAFLAALFALGVLVCIVIGARKLGV **..***. * * * * . .*.****. ** *...
20	CE VVAFLASAFAAALAFIPSGDFDWAHGALMCASSLATAACSASLVLSLLMVVIVTSRKYNI HP NPDNIATPIAASLGDLTILSILALVSSPFYR-HKDSRYLTPLVCLSPAALTPVWVLIQKQ ****.*****.***.***. * * . *... . . . * * * * * . ***.
25	CE NPDNVATPIAASLGDLTTLTLVLAFFGSVFLKAHNTESWLNVIIVIVLFLLLLPFWIKIANE HP SPPIVKILKFGWFPILAMVISSFGGLILSKTVSKQYKGMAIFTPVICGVGGNLVAIQT * ** *... **..***. * *...
30	CE NEGTOETLYNGWTPVIMSLISSAGGFIEATV--RRYHSLSTYGPVLNGVGGNLAAVAQA HP SRISTYLMWSAPGVLPQ--MKKFWPNPCSTFCTSEINSM SARVLLLLLVVPGHLIF-FY **..***. . . . ****. . . . * * . . . *
35	CE SRLSTYFHKAGTVGVLNPNWTVSRF-TSVQRAFFSKEWDSRSARVLLLLLVVPGHICFNFL HP I-IYLVGQSVINSQ--TFVVLYLLAGLIQVTILLYLAEMVRLTWHQALDPDNHCIPYL * * . ***.*...****. . . . * *
40	CE IQLPTLTSKNNVTPHGPLFTSLYMIAAIIQVVILLFVCQLLVALLWKWKIDPDNSVIPYL HP TGLGDLGTGLLALCFPTDWLLKSKAELGGISELASGPP *.*****. . . *
45	CE TALGDLGTGLLFIVFLTTDHPDPKELTSS

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

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example, Accession No. AA334000) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10530> (SEQ ID Nos. 96, 106, and 116)

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Determination of the whole base sequence of the cDNA insert of clone HP10530 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 80-bp 5'-untranslated region, a 1182-bp ORF, and a 95-bp 3'-untranslated region. The ORF codes for a protein consisting of 393 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 46 kDa that was somewhat larger than the molecular weight of 44,912 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 45.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 23. When expressed in COS7 cells, an expression product of about 43 kDa was observed in the supernatant fraction and the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein IG002N01 (GenBank Accession No. AF007269). Table 25 shows the comparison between amino acid sequences of the

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human protein of the present invention (HP) and the A.
thaliana hypothetical protein IG002N01 (AT). Therein, the
marks of -, *, and . represent a gap, an amino acid residue
identical with that of the protein of the present invention,
and an amino acid residue similar to that of the protein of
the present invention, respectively. The both proteins
shared a homology of 27.0% in the N-terminal region of 355
amino acid residues.

Table 25

[illegible]

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

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protein of the present invention.

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<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA
5 insert of clone HP10541 obtained from cDNA library of human
15 stomach cancer revealed the structure consisting of a 7-bp
5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-
untranslated region. The ORF codes for a protein consisting
20 of 196 amino acid residues and there existed a putative
secretory signal at the N-terminus. Figure 37 depicts the
10 hydrophobicity/hydrophilicity profile, obtained by the Kyte-
Doolittle method, of the present protein. In vitro
25 translation resulted in formation of a translation product
of 23 kDa that was somewhat larger than the molecular weight
16 of 21,553 predicted from the ORF. In this case, the addition
of a microsome led to the formation of a product of 20 kDa
30 from which the secretory signal is considered to have been
cleaved and a product of 23 kDa which is considered to have
a sugar chain being attached. Application of the (-3,-1)
35 20- rule, a method for predicting the cleavage site of the
secretory signal sequence, allows to expect that the mature
protein starts from glycine at position 41. In addition,
there exists in the amino acid sequence of this protein one
40 site at which N-glycosylation may occur (Asn-Leu-Thr at
25 position 185).

The search of the protein data base using the amino
acid sequence of the present protein revealed that the
45 protein was similar to the human zymogen membrane protein
(GenBank Accession No. AF056492). Table 26 shows the
30 comparison between amino acid sequences of the human protein
of the present invention (HP) and the human zymogen membrane
50 protein (ZM). Therein, the marks of -, *, and . represent a

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gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.6% in the C-terminal region of 133 amino acid residues.

Table 26

HP	MWRVPGTTRRPVTGESPGMRPEAMLLLTALLGGPTWAGKMYGPGGGKYFS-TTEDYD

ZM	MLTVALLALLCASASGNAIQARSSSYSGEYSGGGKRFSHSGNQLD
HP	HEITGLRVSVGLLLVKSQVVKLGDSWDVKLGALGGNTQEVTLQPGEYITKVFVAFQAFLR

ZM	GPITALRVRVNTYYIVGLQVRYGKVWSDYVGGRRNGDLEEIFLHPGESVIQVSGKYKWLK
HP	GMVMTSKDRYFYFGKLDGQISSAYPSQEGQVLVGIYQYQLLGIKISIGFEWN-YPLEEP

ZM	KLVFVTDKGRYLSFGKDSGTSFNAVPLHPNTVLRFISGRSGSL-IDAIGLEHWDVYPTSCS
HP	TTEPPVNLTYANSPPVGR
ZM	RC

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10550> (SEQ ID Nos. 98, 108, and 118)

Determination of the whole base sequence of the cDNA

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insert of clone HP10550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 241-bp 5'-untranslated region, a 324-bp ORF, and a 86-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA348310) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10590> (SEQ ID Nos. 99, 109, and 119)

Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

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43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10591> (SEQ ID Nos. 100, 110, and 120)

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Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

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of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

Determination of the whole base sequence of the cDNA insert of clone HP01462 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF, and a 477-bp 3'-untranslated region. The ORF codes for a protein consisting of 483 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 41 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 72 kDa that was larger than the molecular weight of 55,838 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 21.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein ZK1058.4 (EMBL Accession No. Z35604). Table 27 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein ZK1058.4 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.6% in the entire region.

Table 27

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HP HPAFHTFCVLLVFGSVSEAKFDDFEDEEDIVEYDDNDFAEFEDMEDSVTSESPQRVIIT
* *
CE
MKIVWIFLIFFIGFAIST
HP EDDE-DETTVELEGQDENQEGDFEDADTQEGDTESEPYDDEEFEGYDKP-----D
* . * . * . * . . . * . . . . . * . * . *
CE DDNEFAEFEDFVGSSTATQAPETQREGEPPVLKQKDDFEZDFGVVEEPEEAKEVREAD
HP TSSSKNKDPTITVDVPAHLQNSWESYYLEILMVTGLLAYIMNYIIGKNKNSRLAQAWFNT
* . . . . * . . . . * . . . . * . . . . * . . . . * . . . . *
CE SDDAAPAQPLKFADVFAHFRSNWASYQVEGIVVLIILITMTNYLIGKTTNASIAQTIFDM
HP HRELLESNFTLVGDDGTNKEATSTGKLNQENEHIYNLNCSGRVCCGMLIQLRPLKQDQL
* * * . * . . . . * . . . . * . . . . * . . . . * . . . . *
CE CRPTLEEQFAVVGDDGTTDLDKMIPSLKHDTDSTFSAWCTGRVNVNSLPLQMKMKVRQDV
HP LNVLARMRPVSDDQVQIKVTMN-DEDMDTYFVAVGTRKALVRLQKEMQDLSEFCSDKPKS
* . . * . * . . . . * . . . . * . . . . * . . . . * . . . . *
CE VSRIMEMFTPSGDKMTIKASLETTNDTDPLIFAVGEKKIASKYFKEMLDLNSFASERKQA
HP GAKYGLPDSLAILSEMGEVTDGMMDTKMVHFLTHYADKIESVHFSQDQSGPKIMQEEOGP
* . . . . * . . . . * . . . . * . . . . * . . . . * . . . . *
CE AQQFNLPASWQVYADQNEVVFSILDPGVVSLLKKHEDAIEFIHISDQFTGPKPAEGESYT
HP LKLPDTRKRTLLFTFNVPGSGNTYPKMEALLPLNMNVIYSIDKAKKFLRNREGCKQADKN
* * . . . * . . . . * . . . . * . . . . * . . . . * . . . . *
CE -RLPEAQRYMEVSNLNLQYLG---QDEESVMEILNLVFIYIDKARKMKLSKDAKVAERR
HP RARVEENFLKLTHTVQRBAQAQRREEKKRAEKERIMNEEDPEKQRRLEEAALRREQKLE
* * . . . * . . . . * . . . . * . . . . * . . . . * . . . . *
CE RKEFEDAFLEKQTHQFRQEAQAQRREEKTRERKQKLMDES DPQRKRELEAKELKREAKA---
HP KRQMKMKQIKVKAM
* * * * . * *
CE -KSPKMKOLVK

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

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example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP02485> (SEQ ID Nos. 122, 132, and 142)

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Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was observed in the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein W01A11.2 (GenBank Accession No. U64852). Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein W01A11.2 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

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15      5      HP      MVEFAPLFMPWERRLQTLAVLQFVFSFLALAEICT-V
      .***.***.***.***. * * . . *
      CE MRLRLSSISGKAKLPDKEICSSVSRI LAPLLVPWKRRL ETLAVMGFIFMWVILPIMDLWV
      HP GFIALLFTRFWLLT VLYAAWYLD RDKPRQGGRIQAI RCWTIWKYMKDYFPISLVKTAE
      * .*. **.*.*. ***.*.* * *.*.....* . * . ***. ***.*.*.***.
20      CE PFHVLFNTRWFWFLVPLYAVVFPYDFDTPKKASRRWNWARREVAWKYFASFYFPLRLIKTAD
      10      HP LDPSRNYIAGFH PHGVLAVGAPANLCTESTGFSSIFPGIRPHLMLTLWFRAPFFRDYIM
      * ..*** * ****.....**.....*****. ****.*.* * * ** *..
      CE LPADRNYYIGSHPHGMFSVGGFTAMSTNATGFPEDKFPGIKSHIMTLNGQFYFPPFRREFGI
      HP SAGLVTSEKESA AHILNRKGGNLLGIIVGGAQEALDARPGSP TLLLRNRKG FVRLALTH
25      * .. *** ..*.. * * . *.*** **.*.*.. ** * **.*. *..
      15      CE MLGGIEVS KESLEYTLTKCGKGRACAIVIGGASEALEAHPNKNTLT LINRRGFCYALKF
      HP GAPLVP IFSFGENDLFDQIPNSSGSWLRYIQNRLQKIMGISLPLFHGRGVF-QYSFGLIP
      ** ***.....*****.* ..***.* ..*.....*.. ****.*.. ** *..*
30      CE GADLVPMYNFGENDL EYQYENPKGSRLREVOEKIKDMFGLCP LLRGRSLFNQYLIGLLP
      HP YRRPITTVVGKPIEVQKTLHPSEEEVNLHQRYIKELCNLF EAHLKLPNIPADQHLFC
      20      *.*.***.*.* * * *.*. *..*.....* ..*.....* ..*.*.*
      CE FRKPVTVMGRPIRV TQTDEPTVEQIDELHAKYCDALYNLF EYKHLHSIPPDTHLIFQ
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Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. D25664) in ESTs, but, since they are
partial sequences, it can not be judged whether or not any
of these sequences codes for the same protein as the protein
of the present invention.

50 <HP02798> (SEQ ID Nos. 123, 133, and 143)
 Determination of the whole base sequence of the cDNA

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insert of clone HP02798 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 31-bp 5'-untranslated region, a 804-bp ORF, and a 301-bp 3'-untranslated region. The ORF codes for a protein consisting of 267 amino acid residues and there existed four putative transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 30,778 predicted from the ORF. When expressed in COS7 cells, an expression product of about 26 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human DHHC-containing cysteine-rich protein (GenBank Accession No. U90653). Table 29 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human DHHC-containing cysteine-rich protein (DH). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.0% in the intermediate region of 100 amino acid residues. The positions of seven cysteines were conserved between the two proteins. The protein of the present invention also had the DHHC (Asp-His-His-Cys) sequence.

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Table 29

HP	MAPWALLSPGVLVRTGHTVLTWGI
5	DH MYKMNICNKPSNKTAPKSVWTAPAQPSGSPSELQGQSRNRNGWSWPPHPLQIVAWLLYL
15	HP TLVLFLHDTLQWEEQGEELLPLTFLLLVLGSLLLYLAVSLMDPGYVNVQQP-QEELK
	* * * * *
	DH PFAVIGFGILVPLLPHEWVPAGYACMGAIFAGHLVVHLTAVSIDPADDNVRDKSYAGPLP
20	HP EEQTAMVPPAIPLRRCRYCLVLQPLRARHCRECRRCVRRYDHCPWMENCVGERNHPLFV
25 * . * . * . * * * *
	DH IFNRSQHAHVIEDLHCNLCNVDVSARSKECSACNKGVCDFDHCKWLNNCVGERNYRLFL
	HP VYLALQLVLLWGLYLAWSGLRFFQPWGLWLRSSGLLPATFLLLSLFLVASLLLVSHLY
	. * . * . *
30	DH HVSASALLGVLLLVLGCHICLRGVLCPHASAQPTL

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D79050) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10041> (SEQ ID Nos. 124, 134, and 144)

Determination of the whole base sequence of the cDNA insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts

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the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

HP	MSTNNMSDPRRPKNVLRYP---PPSECNPALDDPTPDYMNLLGMIFSMCGLMLKLKRWCA
	.****.*...****** *.***.*****.....
CE	MQQNGDPRRTNRIVRYKPLDSTANQQQAISEDPLPEYMNVLGMIFSMCGLMIRMKWCS
HP	WVAVYCSFISFANSRSEDTKQMMSSFMLSISAVVMSYLQNPQPMTPPW
	.. ** *****.*.*.***.*****.***** *..***
CE	WLALVCSCISFANTRTSDDAKQIVSSEFMLSVS AVVMSYLQNPSPFIIPWVTLTQS

Furthermore, the search of the GenBank using the base

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sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10246> (SEQ ID Nos. 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (GenBank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

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of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

Table 31

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HP MTLFHPGNCFALAYFPYFITYKCSGLSEYNAPWKCQAGVTYLFVQLCKMLFLATFFPTW
*****
TM MTLFHPGNCFALAYFPYFITYKCTDLSEYNAPWKCQAGVTYLFVQLCKMLFLATFFPTW
HP EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
*****
TM EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
HP VGARGIEFDWKYIQMSIDSNISLVHYIVASAQVWMITRYDLYHTFRPAVLLLMFLSVYKA
*****
TM VGARGIEFDWKYIQMSIDSNISLGPYIVASAQVWMITRYDLYHTFRPAVLLLMFLRVYKA
HP FVMETFFVHLCSLGSLGWAALLARAVVTGLLALSTLALYVAVVNVHS
*****
TM FVMETFFVHLCSLGSLGWAALLARAVVTGLLALSTLALYVAVVNVHS

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10392> (SEQ ID Nos. 126, 136, and 146)

Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

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consisting of a 24-bp 5'-untranslated region, a 777-bp ORF, and a 726-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

<HP10489> (SEQ ID Nos. 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10519> (SEQ ID Nos. 128, 138, and 148)

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Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

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of the present invention.

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<HP10531> (SEQ ID Nos. 129, 139, and 149)

Determination of the whole base sequence of the cDNA
5 insert of clone HP10531 obtained from cDNA library of human
15 osteosarcoma cell line Saos-2 revealed the structure
consisting of a 55-bp 5'-untranslated region, a 1035-bp ORF,
and a 1092-bp 3'-untranslated region. The ORF codes for a
20 protein consisting of 344 amino acid residues and there
10 existed five putative transmembrane domains. Figure 49
depicts the hydrophobicity/hydrophilicity profile, obtained
by the Kyte-Doolittle method, of the present protein. In
25 vitro translation resulted in formation of a translation
product of high molecular weight.

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15 Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
30 of sequences that shared a homology of 90% or more (for
example, Accession No. R50695) in ESTs, but, since they are
partial sequences, it can not be judged whether or not any
20 of these sequences codes for the same protein as the protein
35 of the present invention.

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<HP10574> (SEQ ID Nos. 130, 140, and 150)

40 Determination of the whole base sequence of the cDNA
25 insert of clone HP10574 obtained from cDNA library of human
stomach cancer revealed the structure consisting of a 210-bp
5'-untranslated region, a 1287-bp ORF, and a 1276-bp 3'-
45 untranslated region. The ORF codes for a protein consisting
of 428 amino acid residues and there existed a putative
30 secretory signal at the N-terminus and one putative
transmembrane domain in the intermediate region. Figure 50
50 depicts the hydrophobicity/hydrophilicity profile, obtained

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by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *D. melanogaster* GOLIATH protein (DM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the *D. melanogaster* GOLIATH protein.

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The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

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primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished

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through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more

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preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides

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capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table 33 below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 33

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) [‡]	Hybridization Temperature and Buffer [†]	Wash Temperature and Buffer [†]
A	DNA : DNA	≥50	65°C; 1×SSC -or- 42°C; 1×SSC, 50% formamide	65°C; 0.3×SSC
B	DNA : DNA	<50	T _B *; 1×SSC	T _B *; 1×SSC
C	DNA : RNA	≥50	67°C; 1×SSC -or- 45°C; 1×SSC, 50% formamide	67°C; 0.3×SSC
D	DNA : RNA	<50	T _D *; 1×SSC	T _D *; 1×SSC
E	RNA : RNA	≥50	70°C; 1×SSC -or- 50°C; 1×SSC, 50% formamide	70°C; 0.3×SSC
F	RNA : RNA	<50	T _F *; 1×SSC	T _F *; 1×SSC
G	DNA : DNA	≥50	65°C; 4×SSC -or- 42°C; 4×SSC, 50% formamide	65°C; 1×SSC
H	DNA : DNA	<50	T _H *; 4×SSC	T _H *; 4×SSC
I	DNA : RNA	≥50	67°C; 4×SSC -or- 45°C; 4×SSC, 50% formamide	67°C; 1×SSC
J	DNA : RNA	<50	T _J *; 4×SSC	T _J *; 4×SSC
K	RNA : RNA	≥50	70°C; 4×SSC -or- 50°C; 4×SSC, 50% formamide	67°C; 1×SSC
L	RNA : RNA	<50	T _L *; 2×SSC	T _L *; 2×SSC
M	DNA : DNA	≥50	50°C; 4×SSC -or- 40°C; 6×SSC, 50% formamide	50°C; 2×SSC
N	DNA : DNA	<50	T _N *; 6×SSC	T _N *; 6×SSC
O	DNA : RNA	≥50	55°C; 4×SSC -or- 42°C; 6×SSC, 50% formamide	55°C; 2×SSC
P	DNA : RNA	<50	T _P *; 6×SSC	T _P *; 6×SSC
Q	RNA : RNA	≥50	60°C; 4×SSC -or- 45°C; 6×SSC, 50% formamide	60°C; 2×SSC
R	RNA : RNA	<50	T _R *; 4×SSC	T _R *; 4×SSC

‡ : The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

† : SSPE (1×SSPE is 0.15M NaCl, 10mM NaH₂PO₄, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

*T_B - T_R : The hybridization temperature for hybrids anticipated to be less than

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50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, $T_m(^{\circ}\text{C}) = 2(\text{\# of A + T bases}) + 4(\text{\# of G + C bases})$. For hybrids between 18 and 49 base pairs in length, $T_m(^{\circ}\text{C}) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\% \text{G+C}) \cdot (600/N)$, where N is the number of bases in the hybrid, and $[\text{Na}^+]$ is the concentration of sodium ions in the hybridization buffer ($[\text{Na}^+]$ for $1\times\text{SSC}=0.165\text{M}$).

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Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

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Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

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Claims

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CLAIMS

1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

2. An isolated DNA coding for the protein according to Claim 1.

3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140.

4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150.

5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eucaryotic cells.

6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.

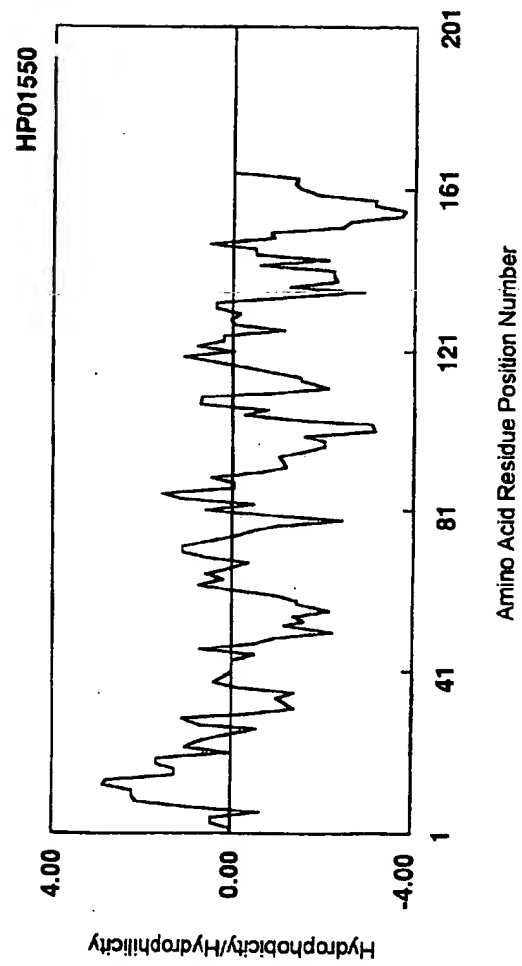


Fig. 1

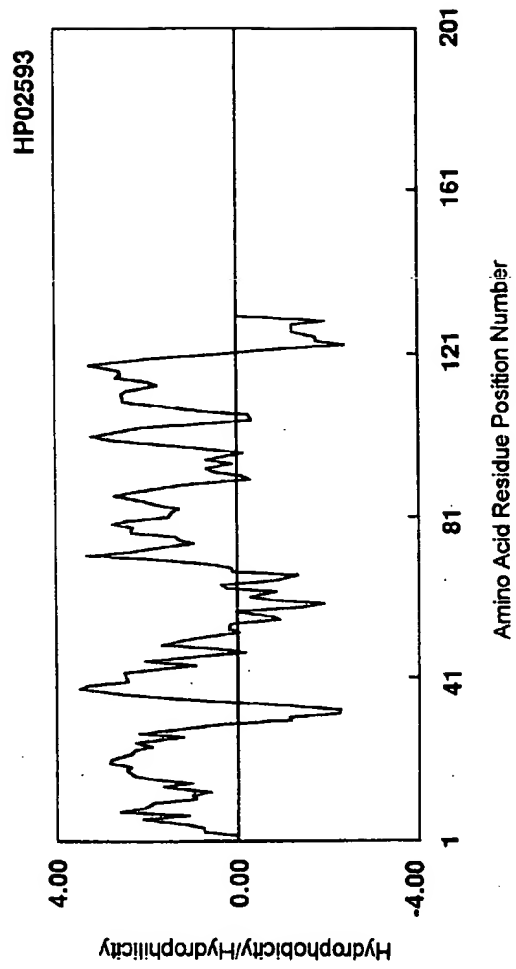


Fig. 2

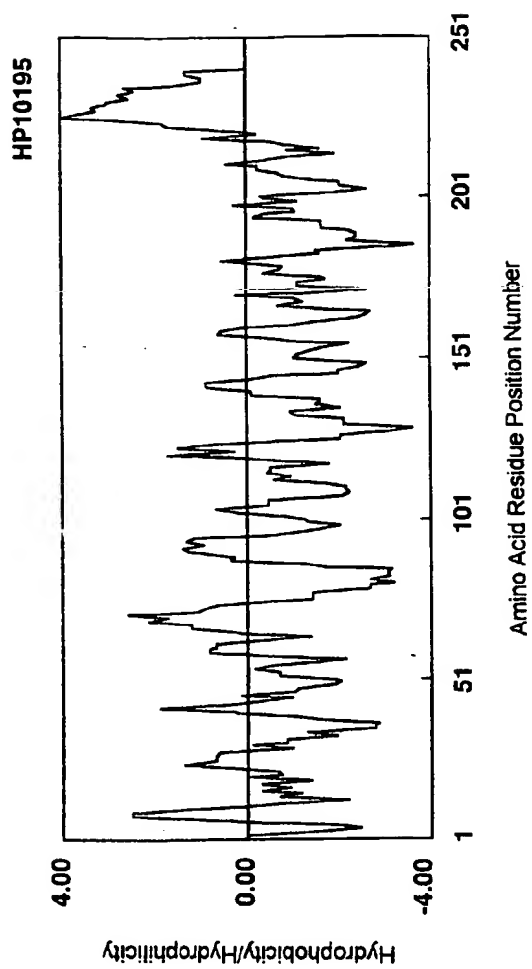


Fig. 3

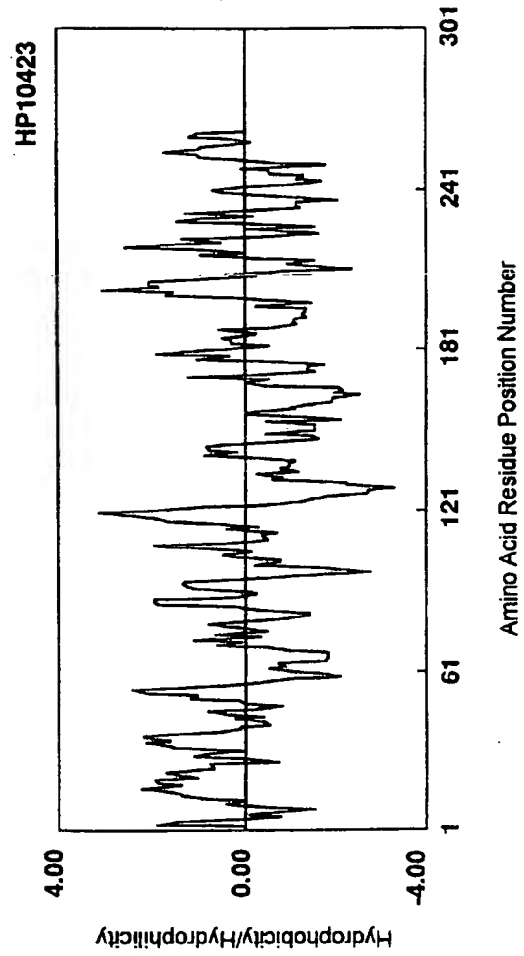


Fig. 4

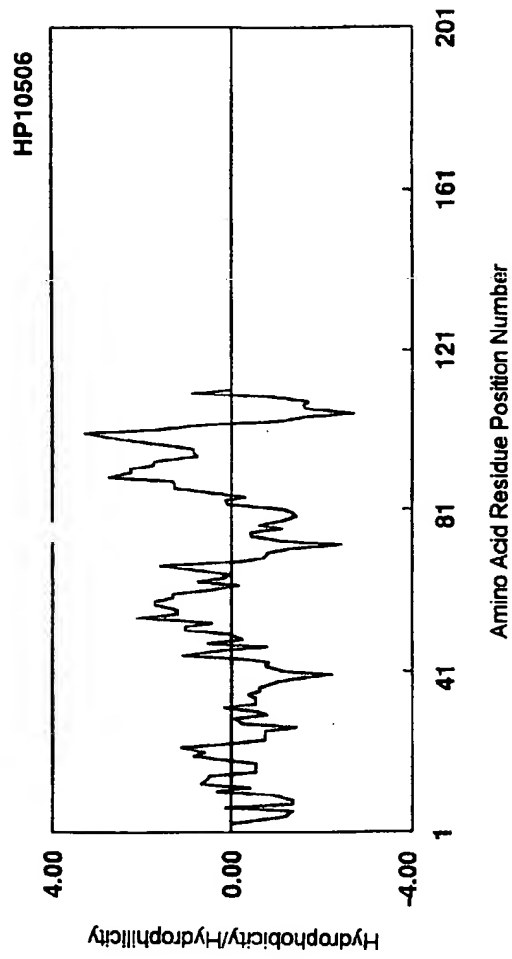


Fig. 5

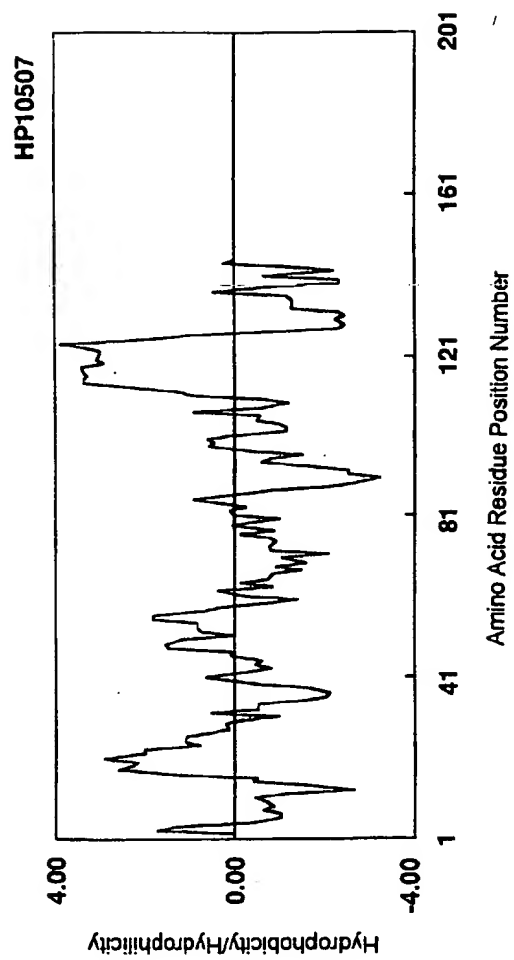


Fig. 6

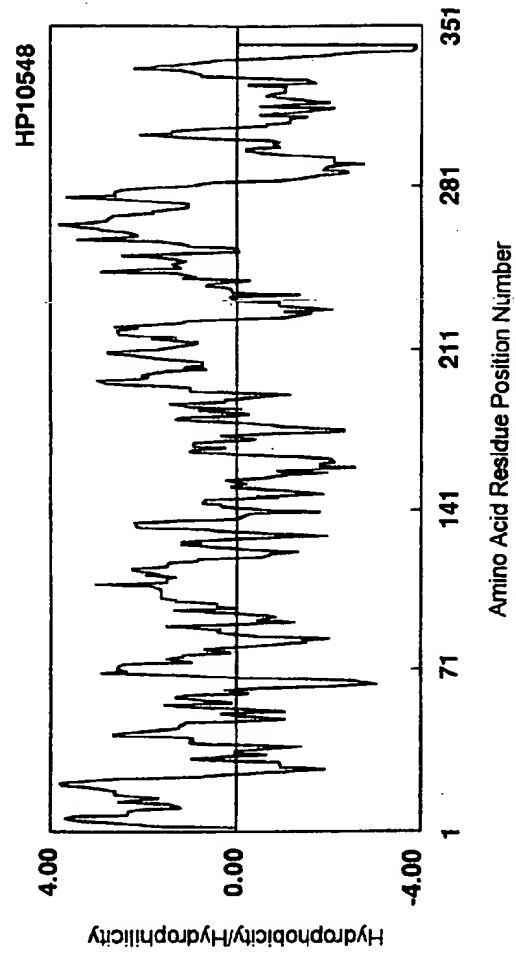


Fig. 7

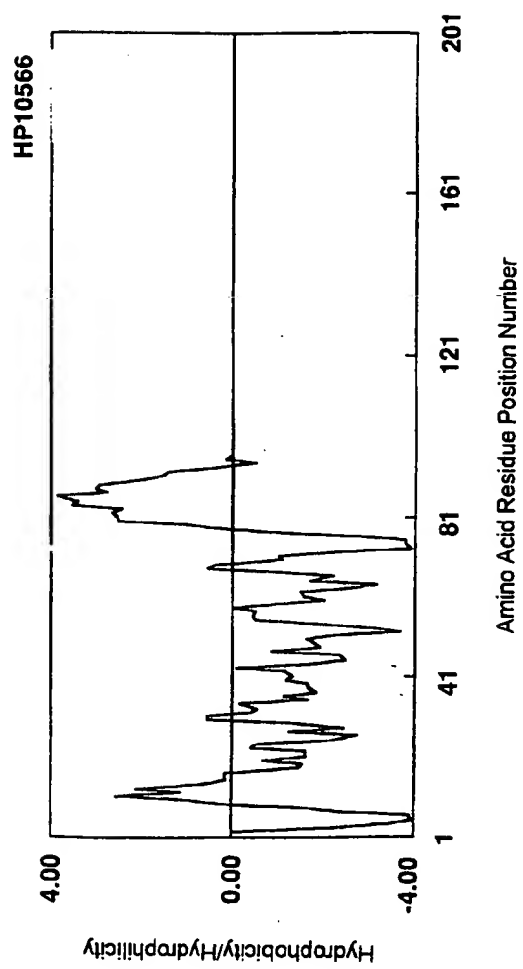


Fig. 8

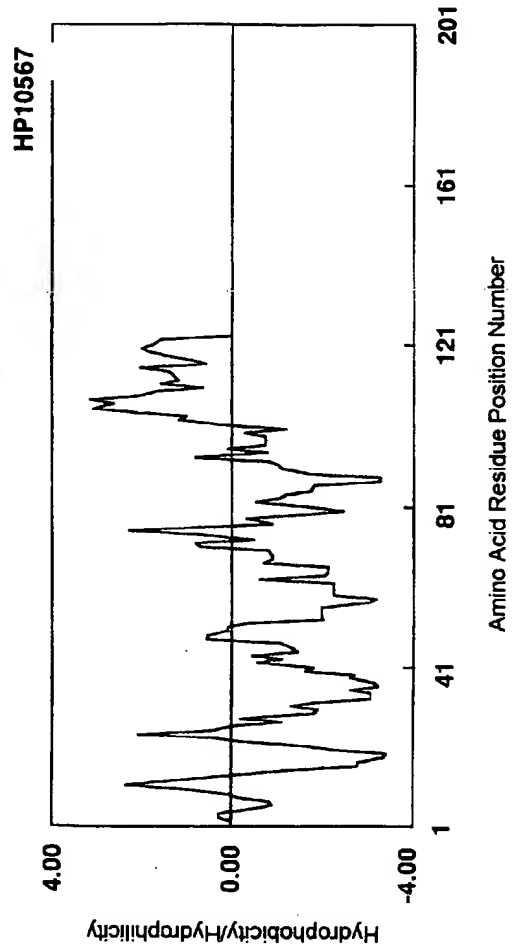


Fig. 9

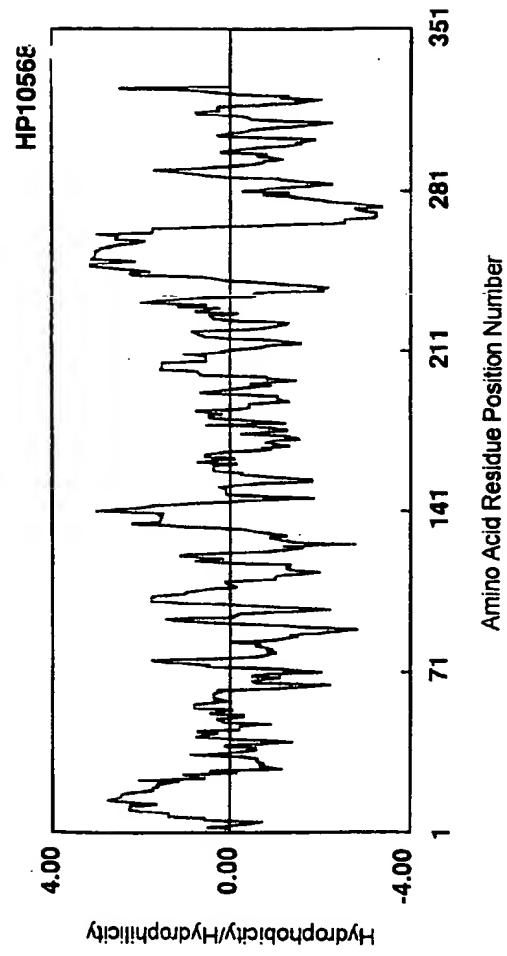


Fig. 10

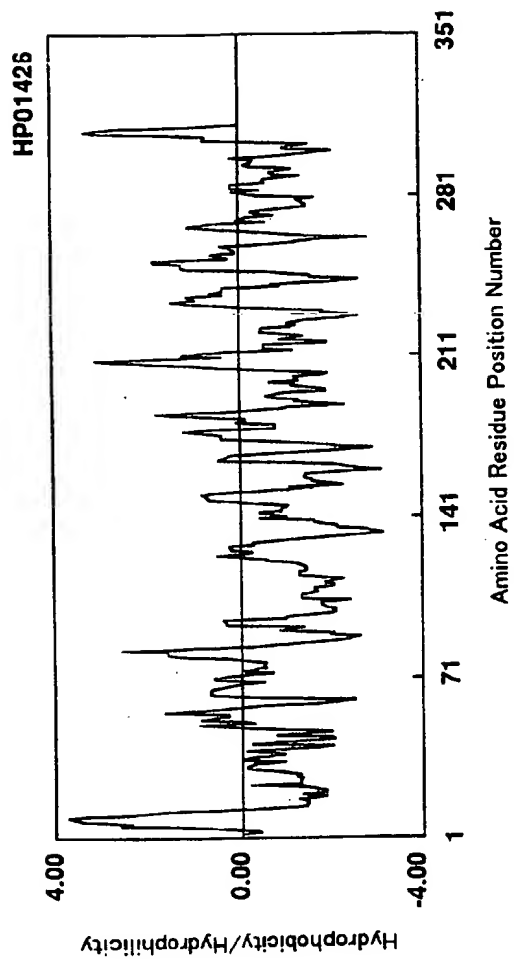


Fig. 11

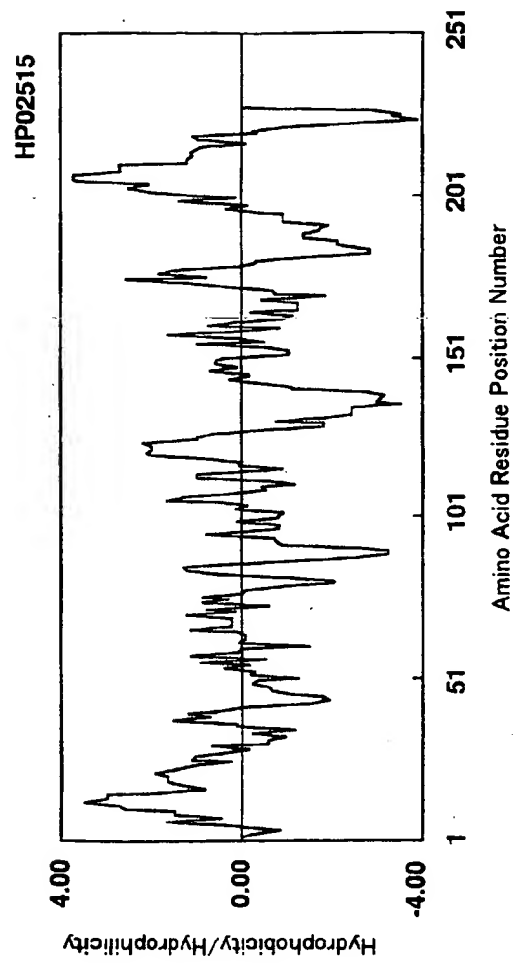


Fig.12

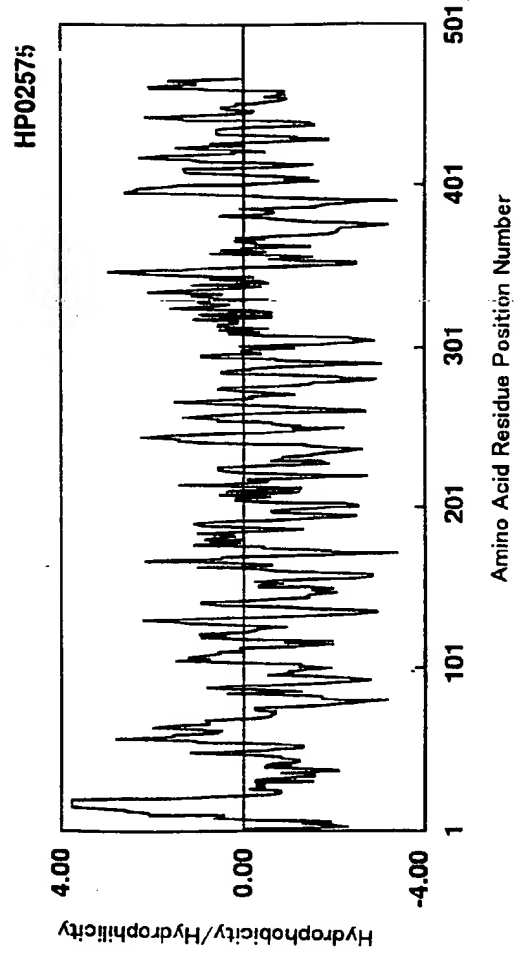


Fig. 13

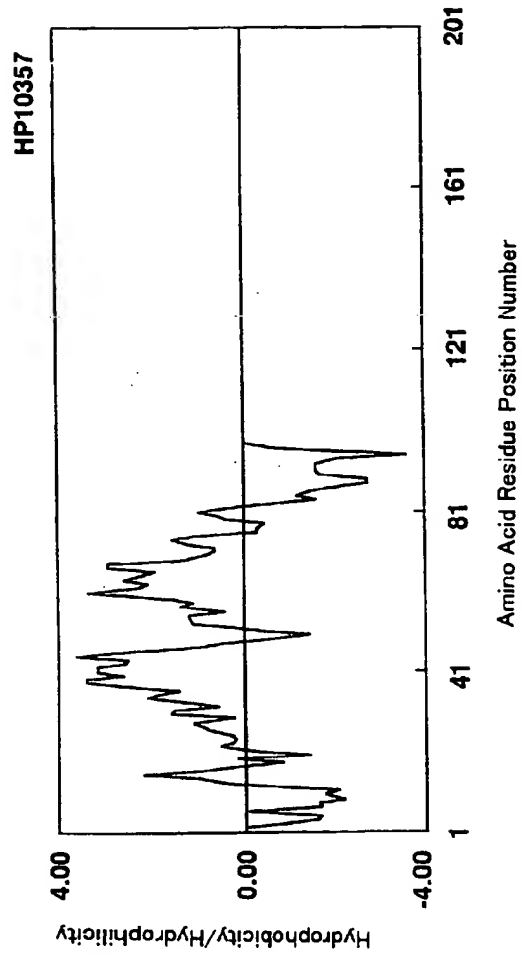


Fig. 14

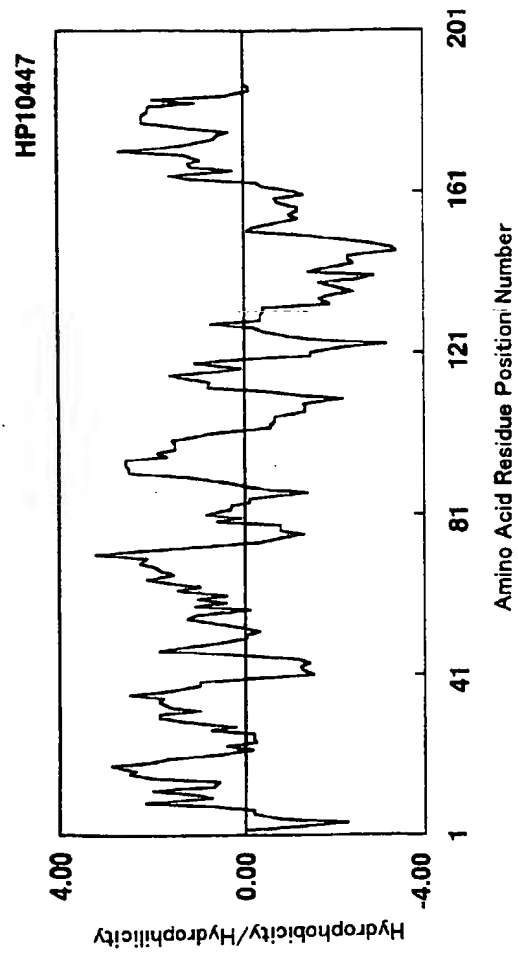


Fig. 15

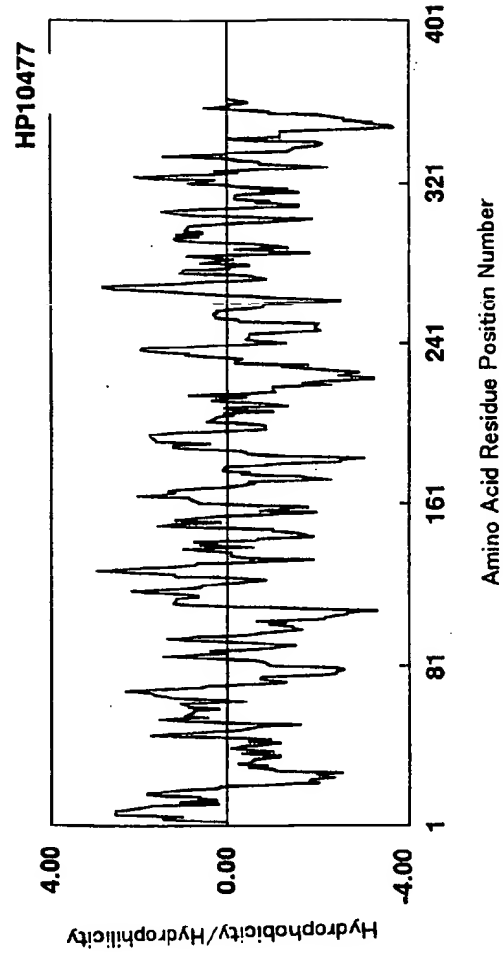


Fig. 16

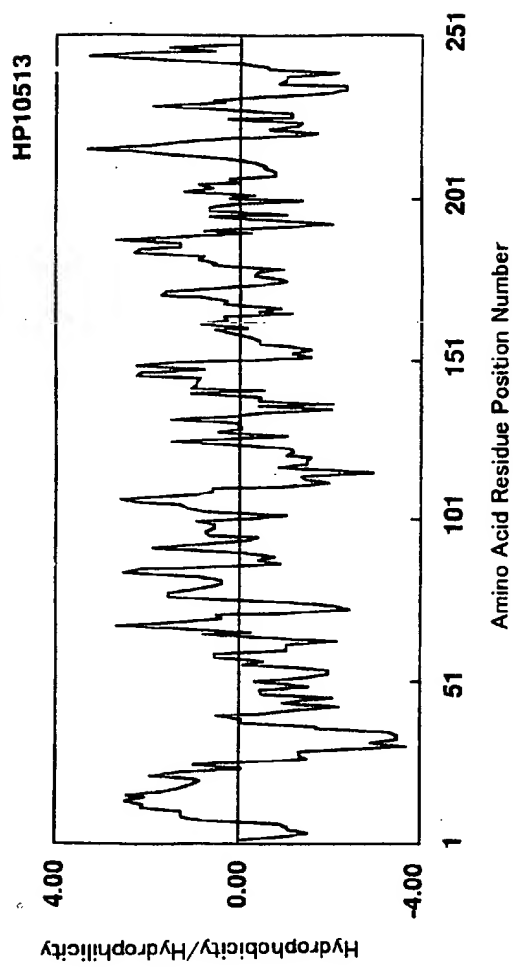


Fig.17

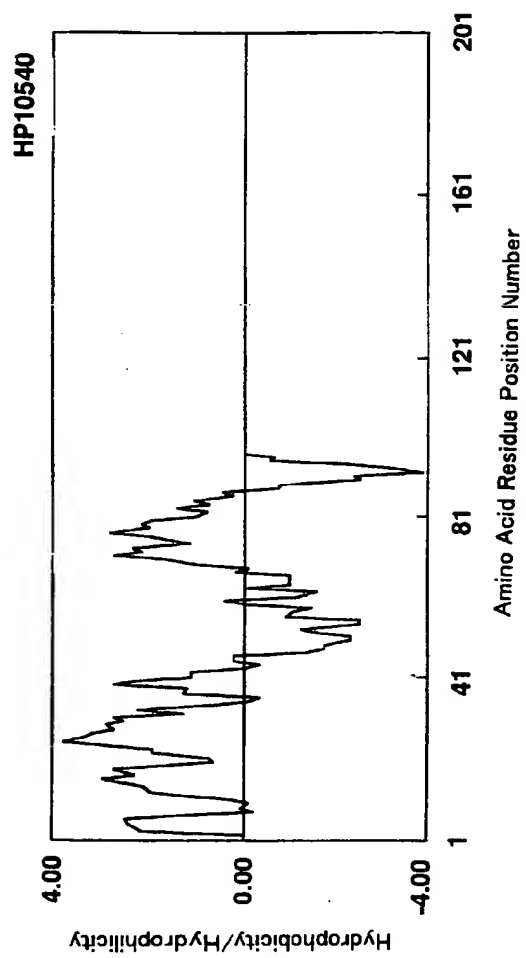


Fig. 18

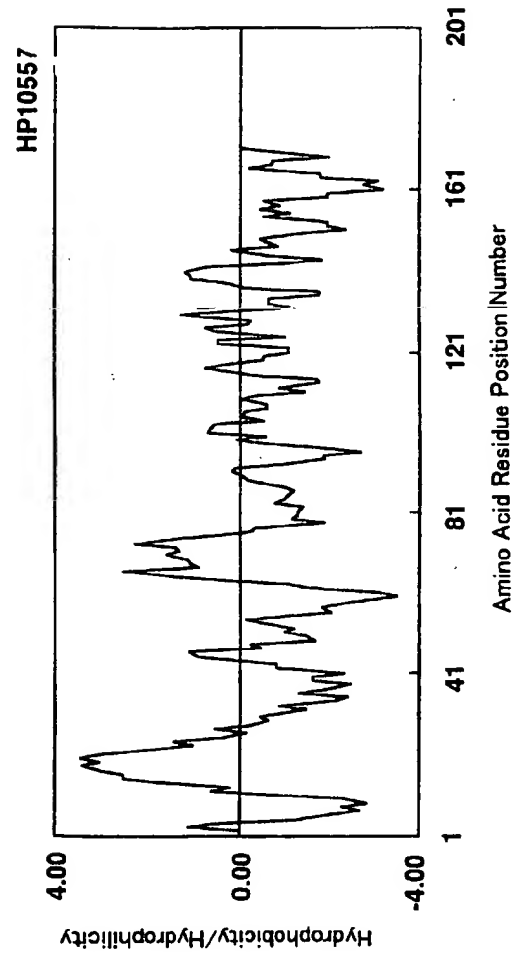


Fig. 19

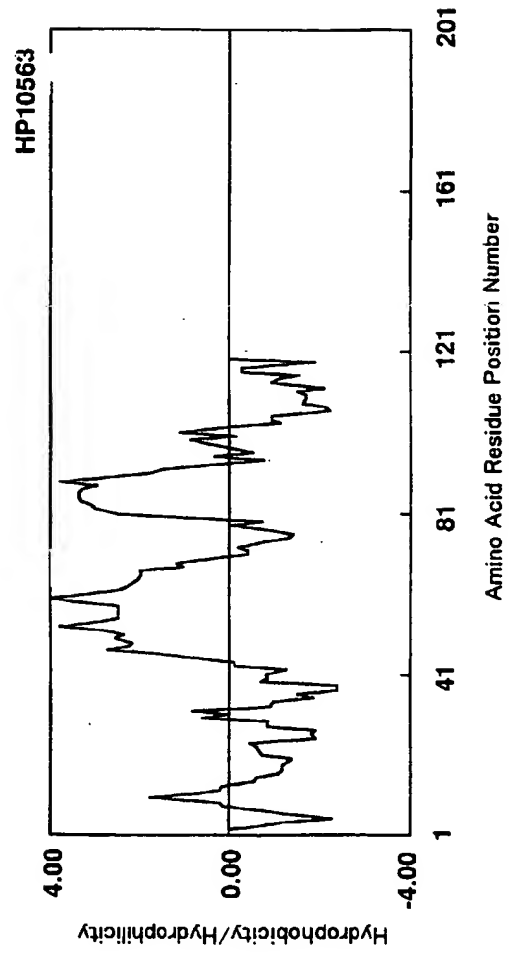


Fig. 20

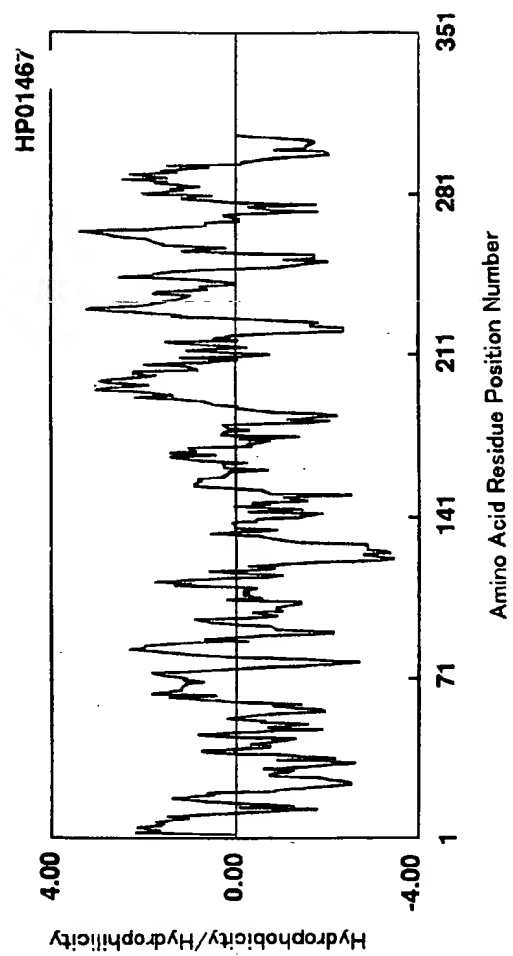


Fig. 21

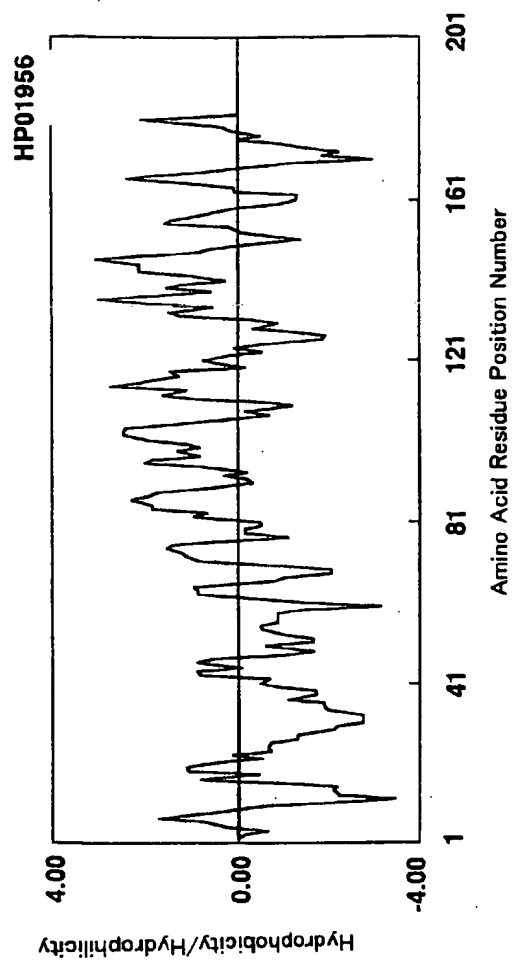


Fig.22

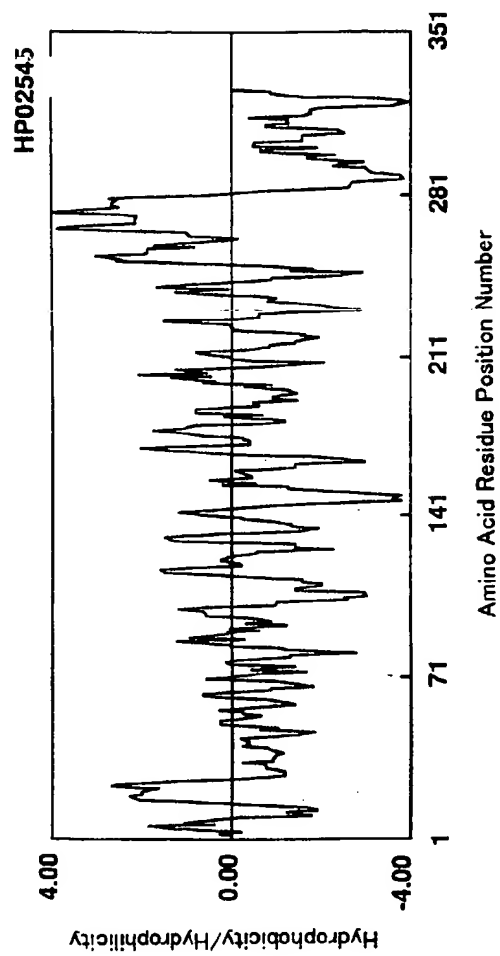


Fig. 23

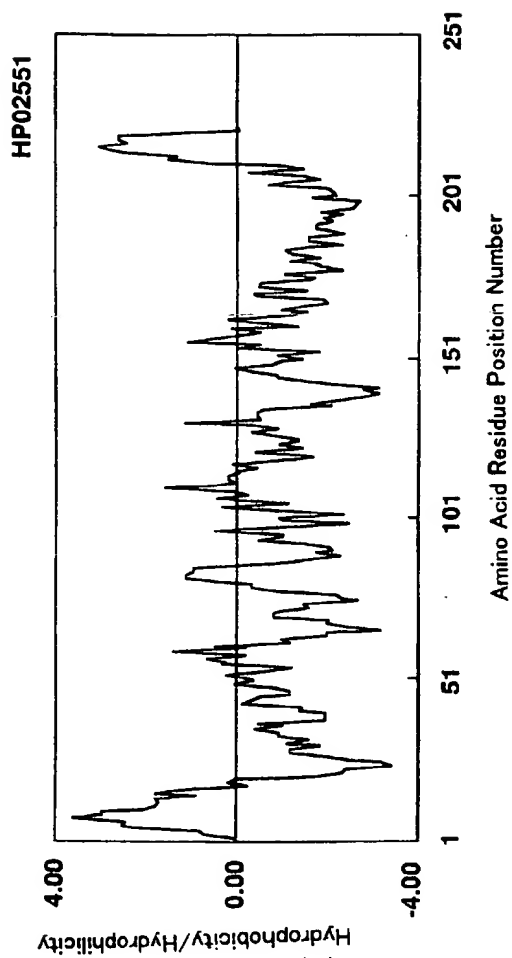


Fig. 24

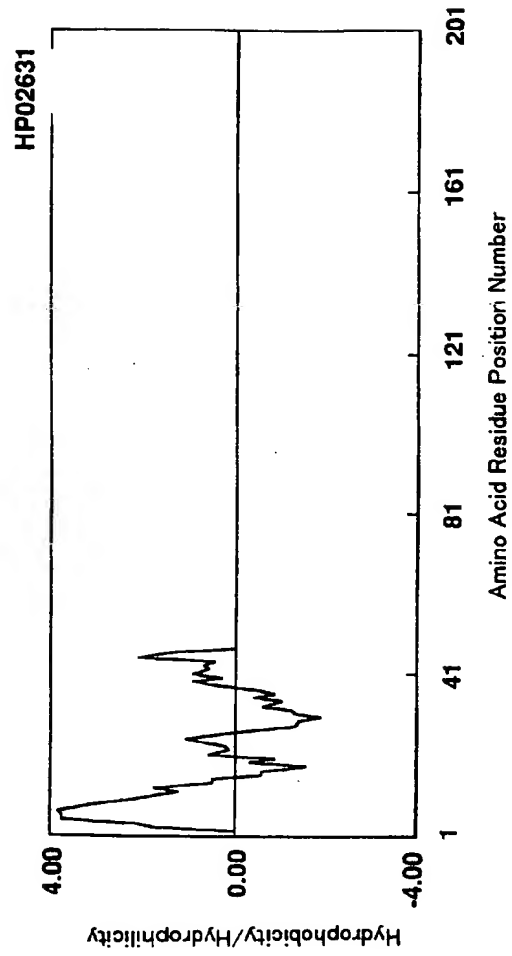


Fig. 25

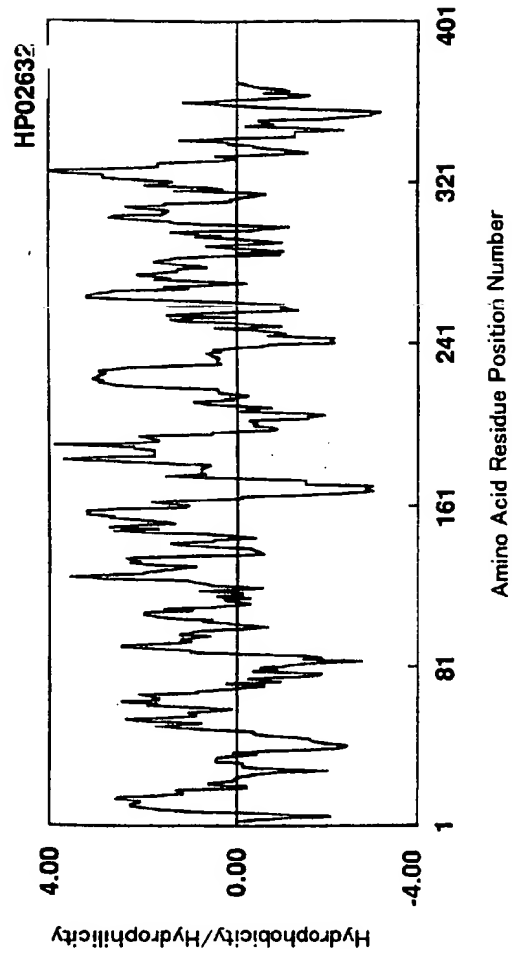


Fig. 26

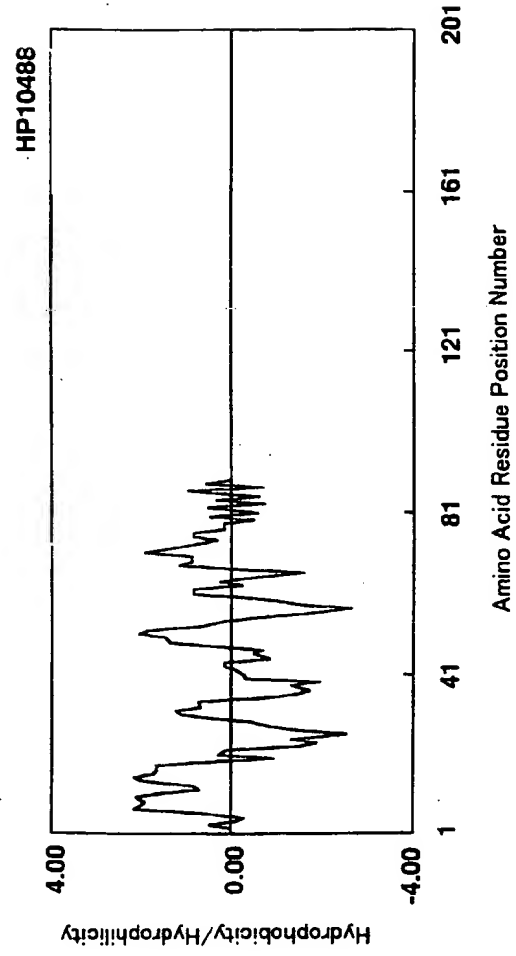


Fig.27

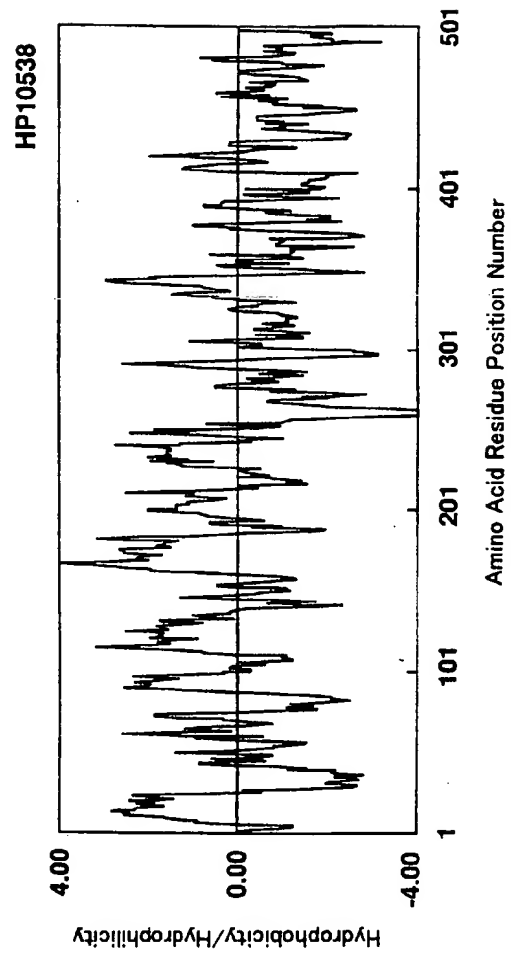


Fig. 28

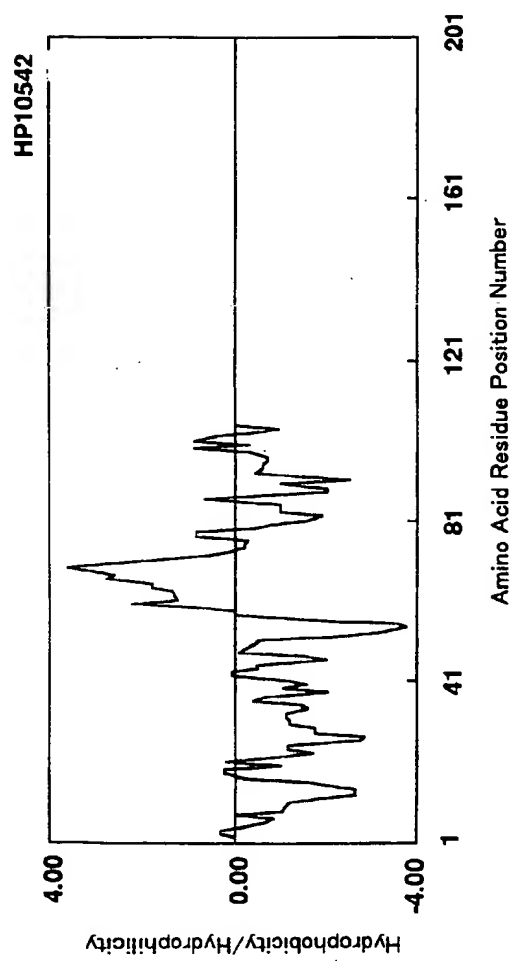


Fig. 29

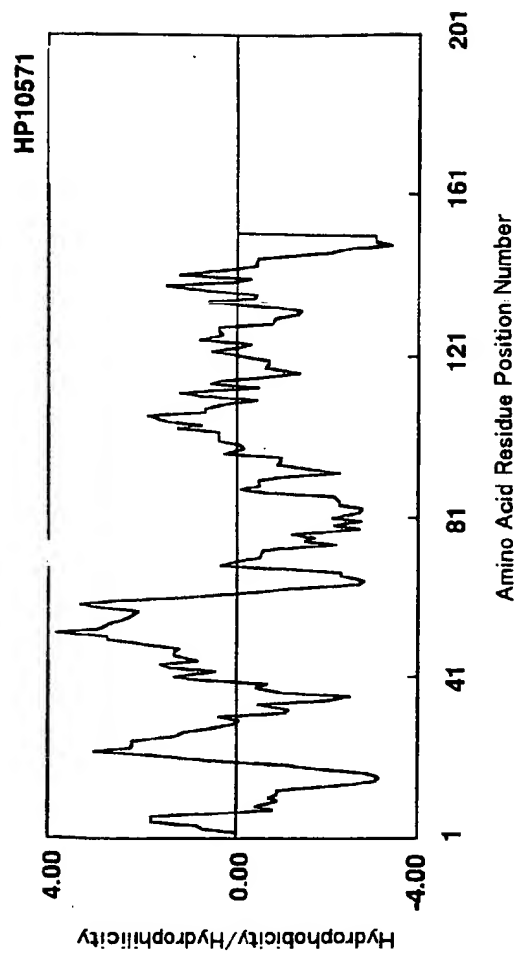


Fig. 30

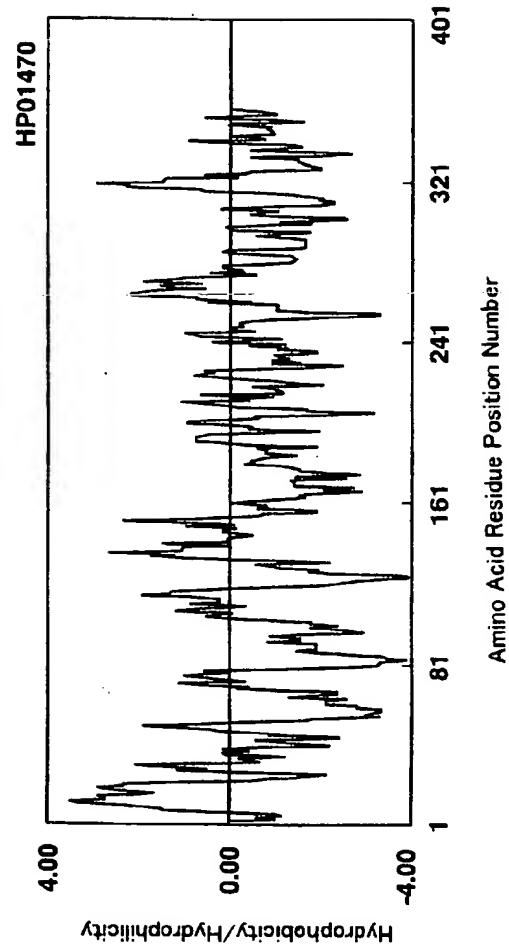


Fig. 31

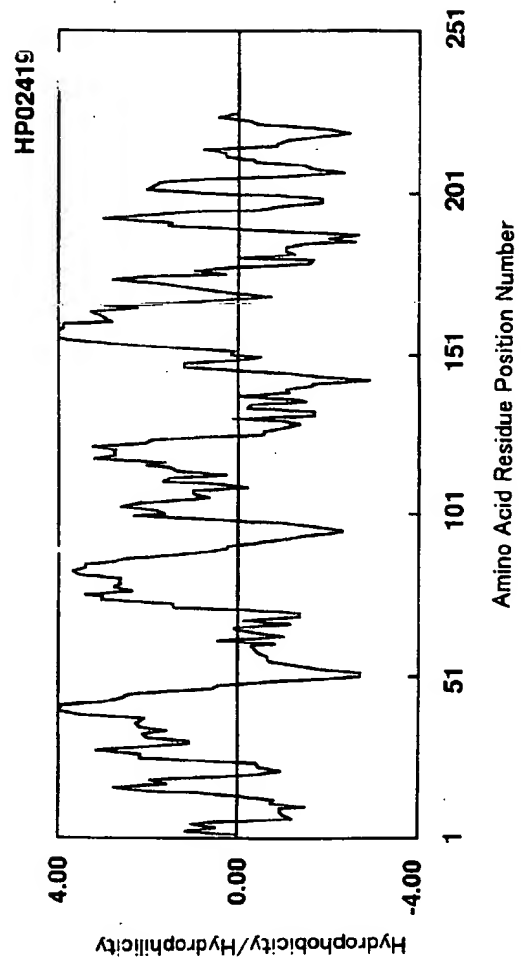


Fig.32

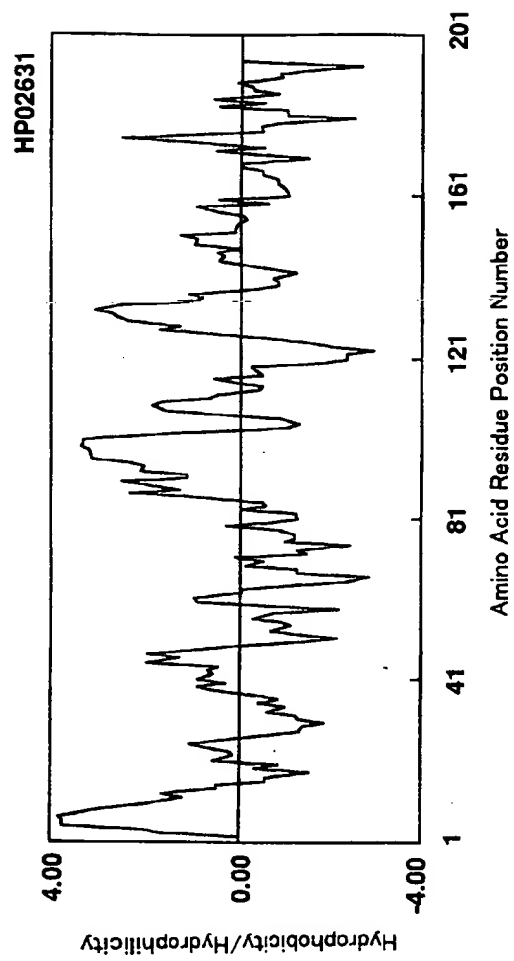


Fig. 33

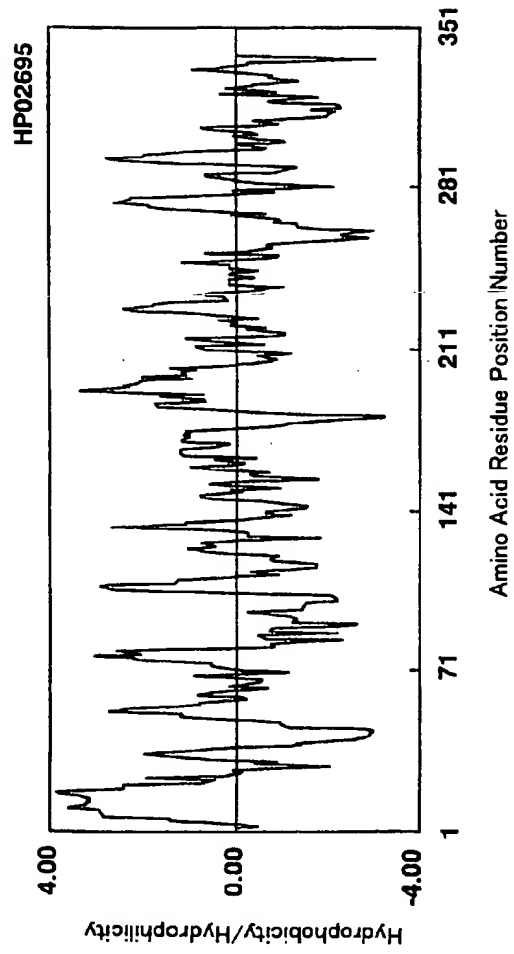


Fig. 34

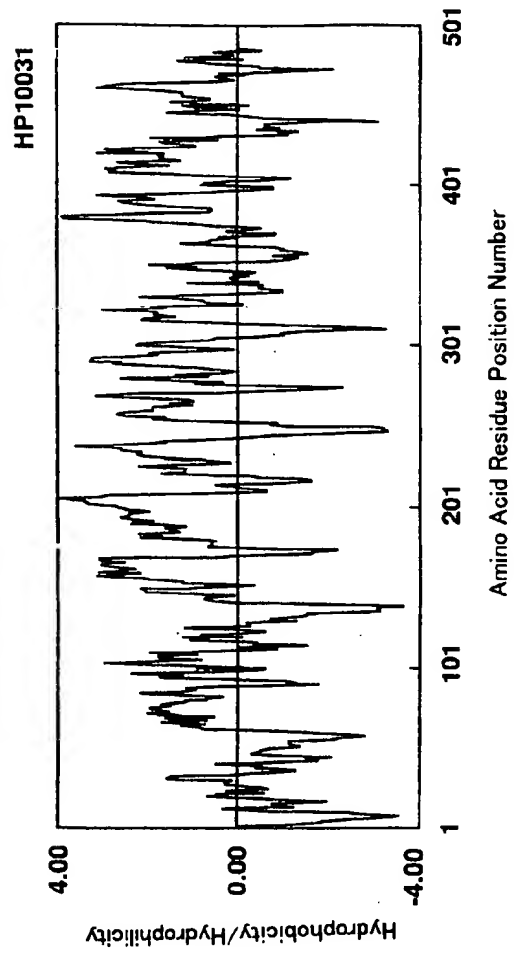


Fig. 35

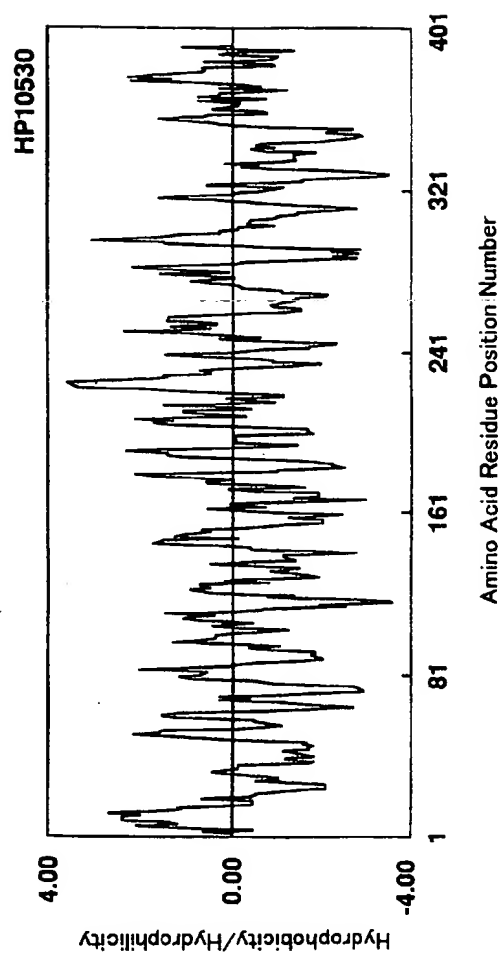


Fig. 36

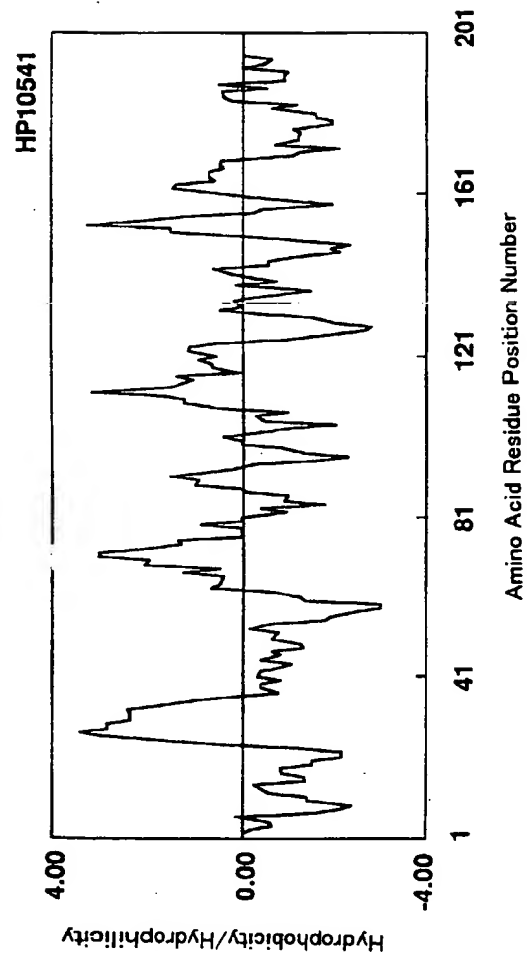


Fig.37

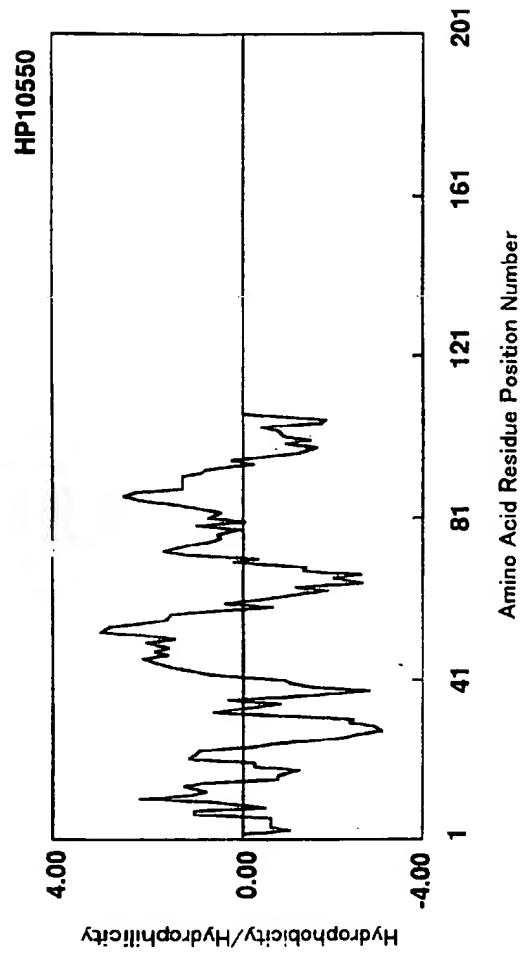


Fig. 38

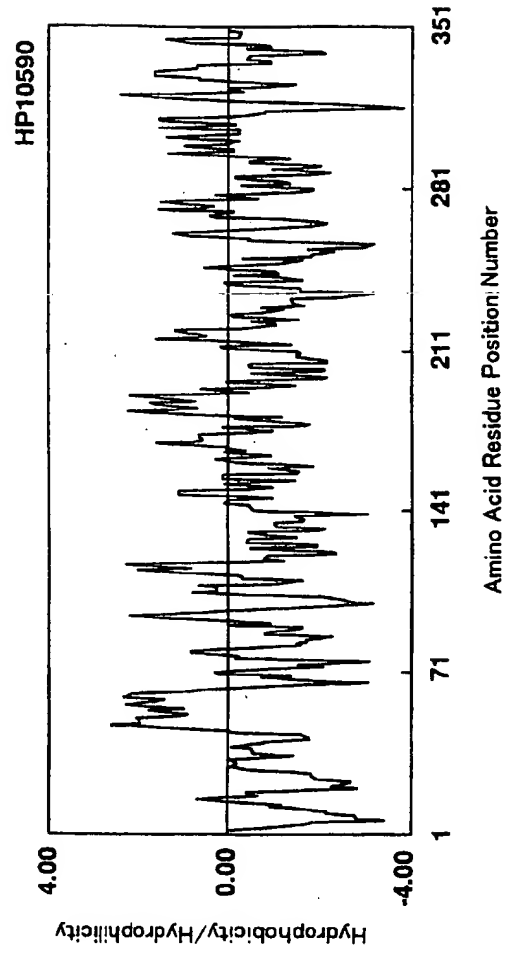


Fig. 39

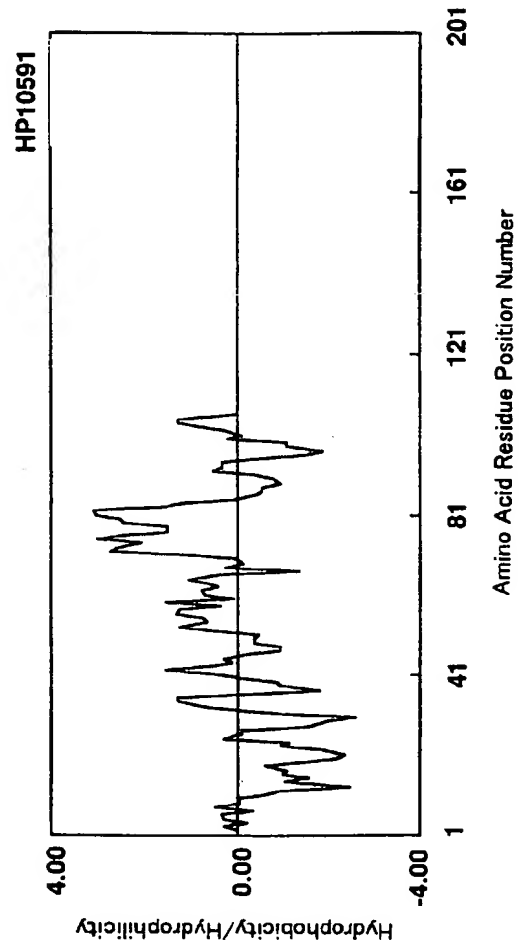


Fig. 40

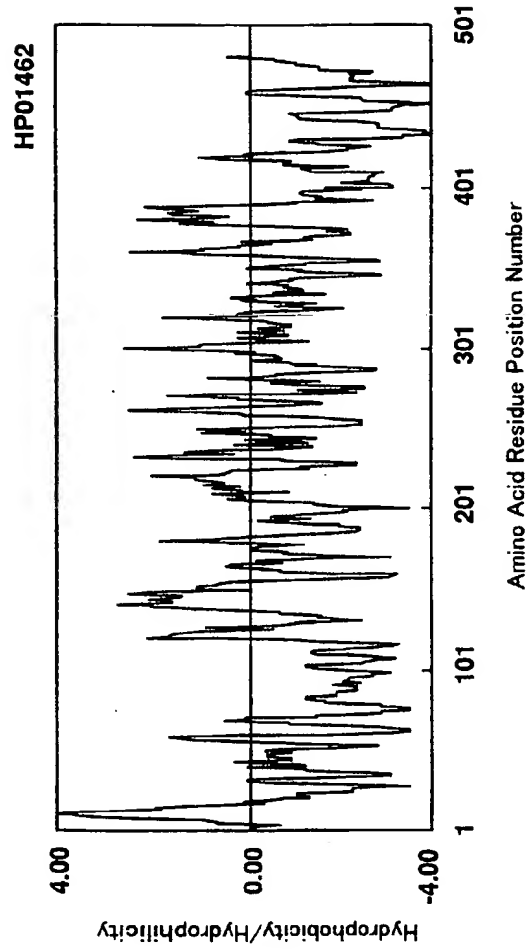


Fig. 41

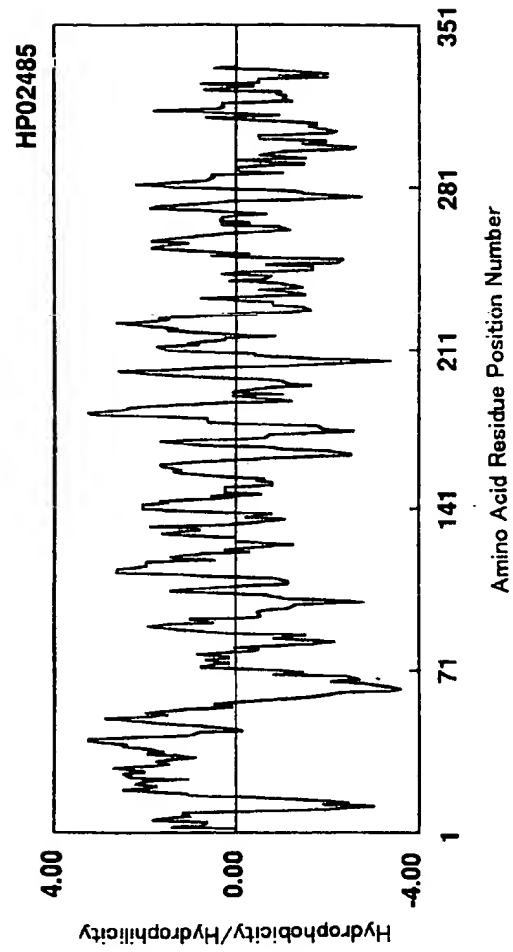


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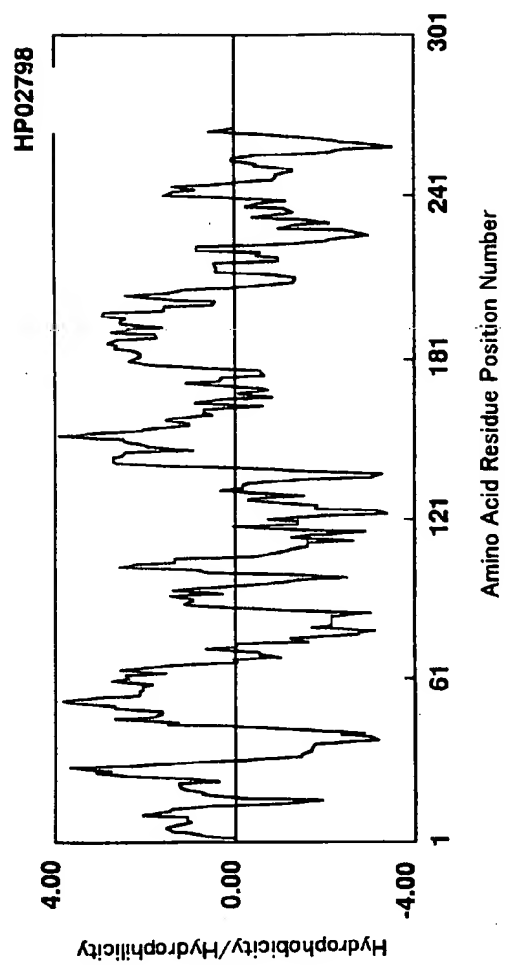


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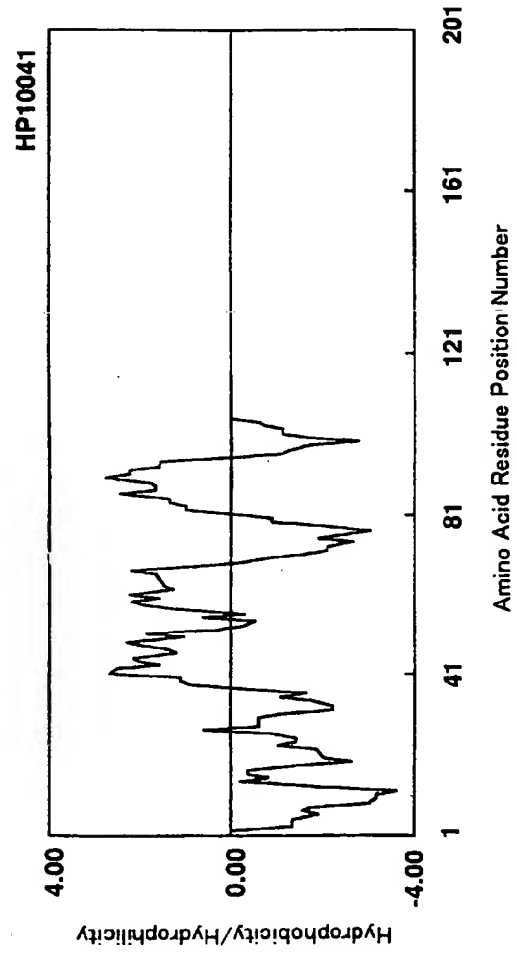


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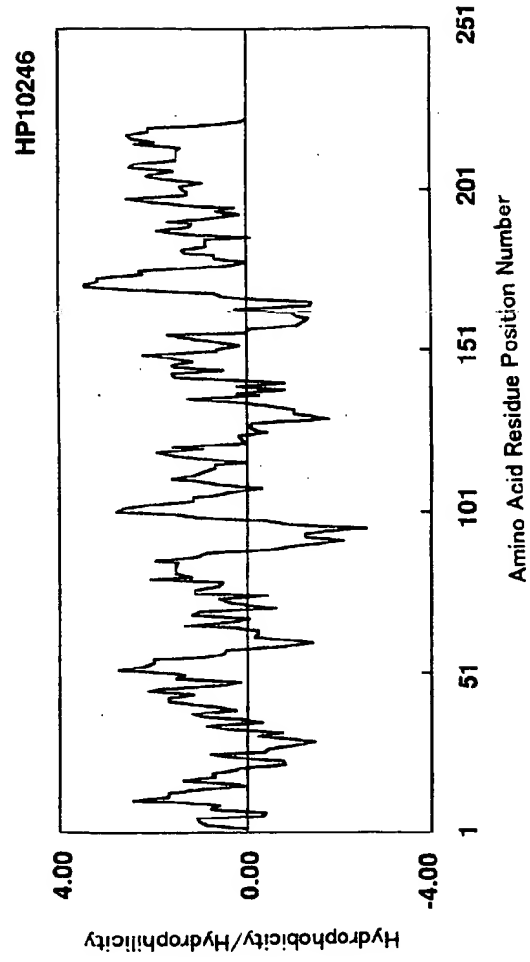


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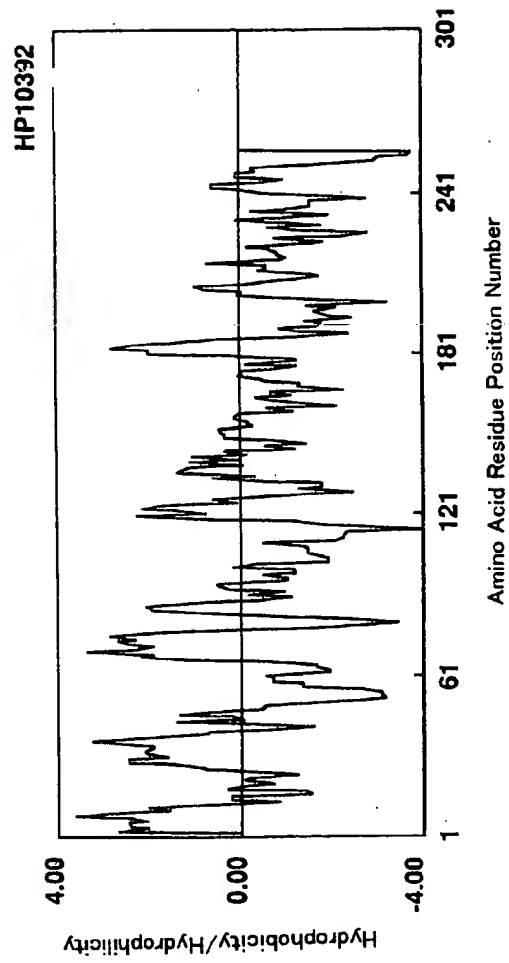


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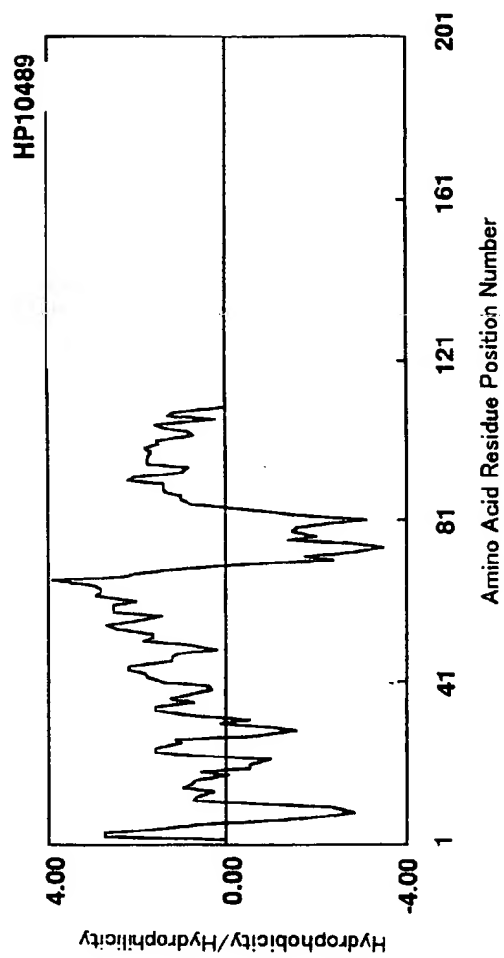


Fig.47

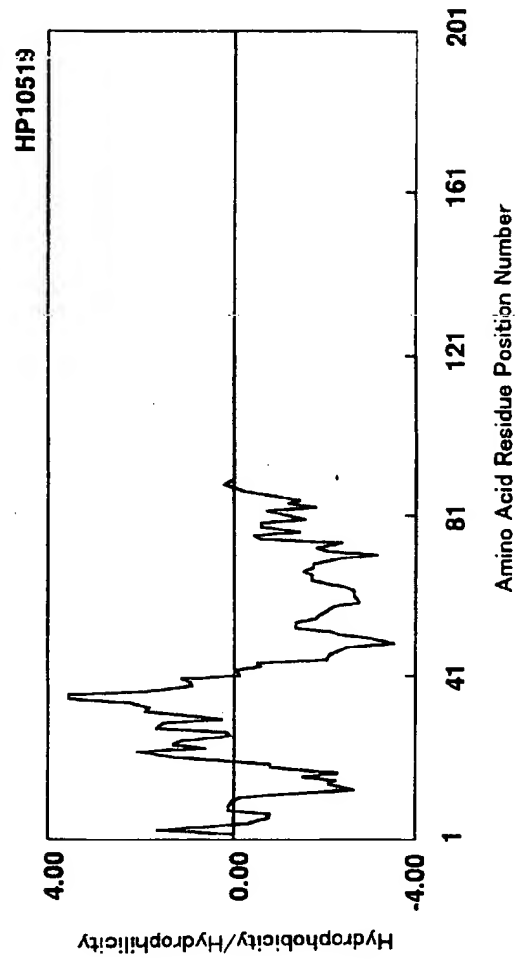


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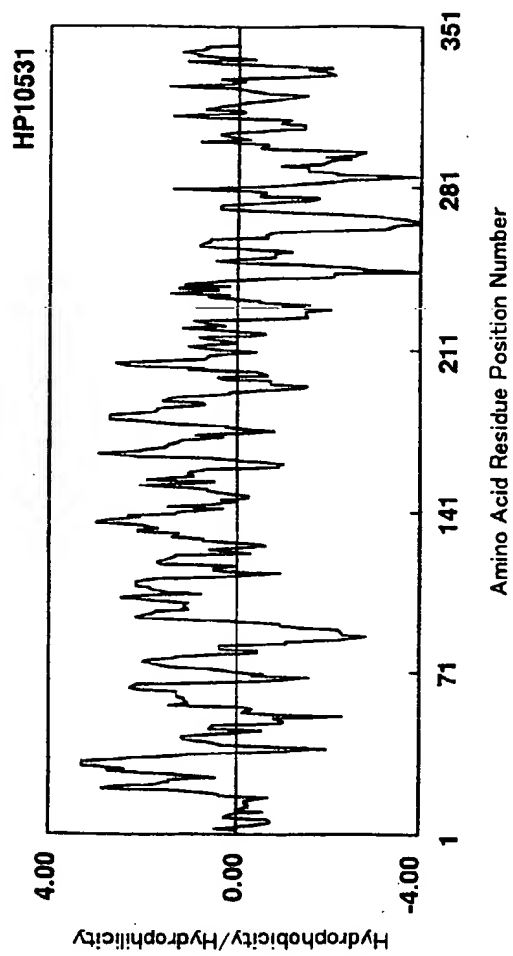


Fig. 49

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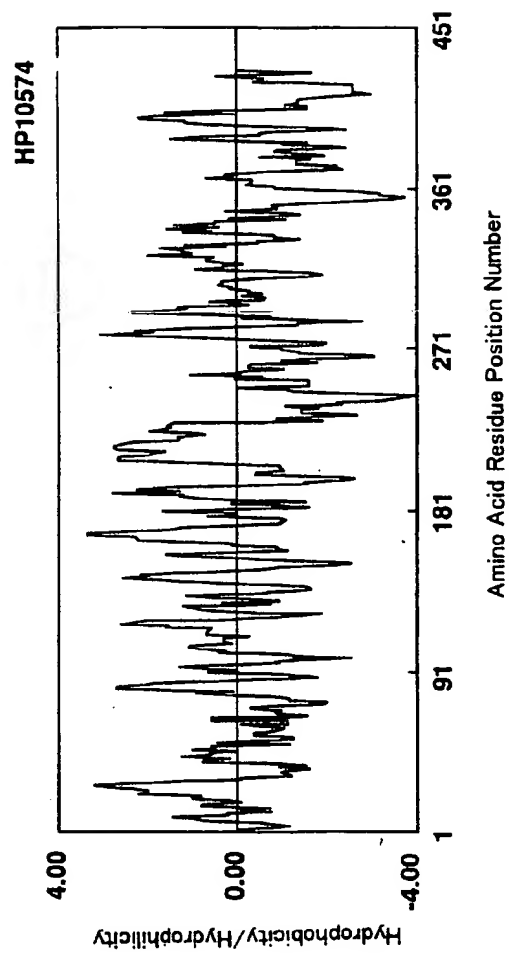


Fig. 50

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<150> JP 10-224105

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 Tyr Cys Ile Ala Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn
 30 50 55 60
 Ala Cys Lys Glu Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser
 65 70 75 80
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 85 90 95
 25 Pro Asn Thr Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp
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 115 120 125
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 165 170 175
 35 Gly Glu Met Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu

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 195 200 205
 Ser Thr Ala Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu
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 35 40 45
 Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr Thr
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 Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser Leu
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 Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys Ser
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 115 120 125
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 130 135 140
 Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn Trp
 35 145 150 155 160

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	Ser	Glu	Gly	Asp	Asn	Ile	Pro	Asp	Ala	Leu	Gly	Leu	Val	Glu	Tyr	Leu
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	Asn	Glu	Trp	Leu	Gln	Ile	Leu	Lys	Pro	Leu	Ser	Asp	Asp	Pro	Thr	Val
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	Ser	Ala	Ser	Arg	Trp	Lys	Ile	Pro	Ser	Ser	Trp	Arg	Leu	Leu	Phe	Gly
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	<213>	Homo sapiens														
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 35 40 45
 Trp Leu Val Glu Glu Phe Val Val Ala Glu Glu Cys Ser Pro Cys Ser
 15 50 55 60
 Asn Phe Arg Ala Lys Thr Thr Pro Glu Cys Gly Pro Thr Gly Tyr Val
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 Glu Lys Ile Thr Cys Ser Ser Ser Lys Arg Asn Glu Phe Lys Ser Cys
 85 90 95
 20 Arg Ser Ala Leu Met Glu Gln Arg Leu Phe Trp Lys Phe Glu Gly Ala
 100 105 110
 Val Val Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln
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	Ile	Pro	Glu	Cys
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	Leu	Gln	Arg	Ala
	Val	His	Gly	Leu
	Leu	His	Tyr	Leu
	Phe	His	Thr	Arg
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	Asn	His	Thr	Phe
	Ile	Val	Leu	His
	Leu	Val	Leu	Gln
	Gly	Met	Val	Tyr
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	Trp	Glu	Val	Phe
	Gly	Tyr	Cys	Gln
	Glu	Leu	Glu	Leu
	85	90	95	
	Ser	Leu	His	Tyr
	Leu	Leu	Leu	Pro
	Tyr	Leu	Leu	Gly
	Val	Asn	Leu	
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	Phe	Phe	Phe	Thr
	Leu	Thr	Cys	Gly
	Thr	Asn	Pro	Gly
	Ile	Ile	Thr	Lys
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	Leu	Phe	Leu	His
	Val	Tyr	Glu	Phe
	Asp	Glu	Val	Met
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	Val	Arg	Cys	Ser
	Thr	Cys	Asp	Leu
	Arg	Lys	Pro	Ala
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	Cys	Ser	Val	Cys
	Asn	Trp	Cys	Val
	His	Arg	Phe	Asp
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	His	His	Cys	Val
	Trp	Val	Asn	Asn
	Cys	Ile	Gly	Ala
	Trp	Asn	Ile	Arg
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	Tyr	Phe	Leu	Ile
	Tyr	Val	Leu	Thr
	Leu	Thr	Ala	Ser
	Ala	Ala	Ala	Thr
	Val	195	200	205
25	Ala	Ile	Val	Ser
	Thr	Thr	Phe	Leu
	Val	His	Leu	Val
	Val	Met	Ser	Asp
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	Leu	Tyr	Gln	Glu
	Thr	Tyr	Ile	Asp
	Asp	Leu	Gly	His
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	Gly	Phe	Val	Val
	Val	Leu	Ser	Phe
	Leu	Leu	Gly	Gly
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	Tyr	Leu	Leu	Phe
	Val	Leu	Tyr	Leu
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	Gln	Thr	Thr	Asn
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 35 40 45
 Leu Glu Lys Glu Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Glu
 50 55 60
 Lys Glu Leu Lys Phe Leu Arg Gln Glu Asn Arg Lys Asn Met Leu Leu
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 Leu Ile Trp Gln Gln Met Lys Ser Glu Asn Glu Arg Leu Gln Glu Glu
 50 55 60
 Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Glu Phe Leu Gln Lys Ser
 10 65 70 75 80
 His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu Gly Gly Gln Ile Lys
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 30 Thr Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro
 50 55 60
 Gly Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly
 65 70 75 80
 His Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln
 35 85 90 95

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 Pro Ser Asp Thr Gly Thr Tyr Leu Cys Gln Val Asn Asn Pro Pro Asp
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 Ser Thr Ala Leu Arg Cys Ser Ser Ser Glu Gly Ala Pro Lys Pro Val
 10 165 170 175
 Tyr Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser
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 Met Val Gln Asp Glu Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser
 195 200 205
 15 Leu Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly
 210 215 220
 Ser Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly
 225 230 235 240
 Arg Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Leu
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 Ser Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg Gly Lys
 260 265 270
 Lys Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile
 275 280 285
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	cagattctca acgtgtccaa gctgagccct gaggaggctc agaaagaacta tgaacactta	240
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	cttgttctca caggaaacac agtcattttt gcaactatac taggcttttt cttggtcttt	360
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	cccttcacag atgtagtcaac tacaatctct aaattggcaa atccatcgga tagaaaagtg	120
	tgtttcaaa tgaaagactac agcacctcgc cggtaactgtg tgaggcccaa cagtgggaatt	180
	attgacctag ggtcaactgt gactgtttca gtaatgctac agccctttga ctatgatccg	240
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		tgcgtatttg aaatgcccc tgaaatgat aaattgaatg atatggaaac tagcaaaagct	420
		gttccactga atgcattcaa gcaagatgga cctatgccaa aaccacacag tgtttcactt	480
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caccgcctgt tgaagacctg ctggagctgt cgcgtgcttt ctgggttggg gotgatgggg	180
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gagaaatca catgcagctc atctaagaga aatgagttca aaagctgccg ctacgctttg	300
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gcttgtcttg tcatcttcg tcagcgacaa ttggacagaa aggtctctga aaaggtccgg	420
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ttttcctgta taattccaga atgtcttcag agagccgtgc atggattgct tcattacctt	180
ttccatacga gaaaccacac cttcattgtc ctgcacctgg tcttgcaagg gatggtttat	240
actgagtaca cctgggaagt atttggctac tgtcaggagc tggagtgtc cttgcattac	300
35 cttctttctg cctatctgct gctaggtgta aacctgttt tttccacct gacttgtgga	360

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	accaaactctg gcattataac aaaagcaaat gaattattat ttcttcactgt ttatgaattt	420
	gatgaagtga tgtttccaaa gaacgtgagg tgctctactt gtgatttaag gaaaccagct	480
	cgatccaagc actgcagtgt gtgtaactgg tgtgtgcacc gtttcgacca tcaactgtgtt	540
	tgggtgaaca actgcactgg ggcttggaac atcaggtaact tctcateta cgtcttgacc	600
5	ttgacggcct cggctgcccac cgtcgccatt gtgagcacea cttttctgggt ccacttggtg	660
	gtgatgtcag atttatacca ggagacttac atcgatgacc ttggacacct ccactgttatg	720
	gacacggctt ttcttattca gtacctgttc ctgacttttc cacggattgt ctteatgctg	780
	ggctttgtcg tggttctgag ctctctctcg ggtggctacc tgttgtttgt cctgtatctg	840
	ggggccacca accagactac taacgagtgg tacagagggtg actgggctcg gtgccagcgt	900
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	aagaaacaaag aa	1032
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	aagctgtccc agtgtcggag agacctggag gccgtgaact ccagactcca cagccgggag	120
	ctgagcccag agggcaggag gtcctcggag aaggagaaaa acagcctaatt gaacaaagcc	180
	tccaaactacg agaagggaact gaagtttctt cggcaagaga accggaagaa catgctgctc	240
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25	<210> 19	
	<211> 372	
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	aagcttcgat tcgaaactta tcagttgata tggcagcaga tgaatctga aaatgagcga	180
35	ctacaagagg aattaaataa aaacttgttt gacaatctga ttgaatttct gcaaaaatca	240

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	cattctggat tccagaagaa ttcaagagac ttggggcggc aaataaaact cagagaaatt	300
	ccaactgctg ctcttgttct tggatatat gcgtatgctt gttcatgcat gcctctctgt	360
	gtatttcggt tt	372
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	gccgagctga cctgcaccta cagcacgtcg gtgggagaca gcttcgccct ggagtgagc	180
	tttgtgcagc ctgggaaacc catctctgag tcccatccaa toctgtactt caccaatggc	240
15	catctgtatc caactggtc taagtc aaag cgggtcagcc tgcctcagaa cccccccaca	300
	gtgggggtgg ccacactgaa actgactgac gtccaccct cagatactgg aacctactc	360
	tgcacaagca acaaccacc agattttctac accaatgggt tggggotaat caaccttact	420
	gtgctggttc cccccagtaa tcccttatgc agtcagagtg gacaaacctc tgtgggaggc	480
	tctactgcac tgagatgcag ctcttcgcag ggggctccta agccagtgt caactgggtg	540
20	cgtcttgaa ctttctctac acctctctct ggcagcatgg ttcaagatga ggtgtctggc	600
	cagctcattc tcaccaacct ctccctgacc tctcgggca cctaccgctg tgtggccacc	660
	aaccagatgg gcagtgcatc ctgtgagctg accctctctg tgaccgaacc ctcccaaggc	720
	cagtggtggc gagctctgat tgggtgctc ctgggcgtgc tgttgctgct agttgctgct	780
	ttctgctctg tcaggttcca gaaagagagg gggagaagc ccaaggagac atatgggggt	840
25	agtgccttc gggaggtatc catcgtctct gggatctctg agcacacttg tatgagggct	900
	gattctagca aggggttctt ggaaagacc tegtctgcca gcaccgtgac gaccaccaag	960
	tccaagctcc ctatggtcgt g	981
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30	<211> 510	
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	<213> Homo sapiens	
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5 Met Ala Lys Tyr Leu Ala Gln Ile Ile Val Met Gly Val Gln Val
1 5 10 15
gtg gcc agg gcc ttt gca cgg gcc ttg cgg cag gag ttt gca gcc agc 158
Val Gly Arg Ala Phe Ala Arg Ala Leu Arg Gln Glu Phe Ala Ala Ser
20 25 30
10 cgg gcc gca gct gat gcc cga gga cgc gct gga cac cgg tct gca gcc 206
Arg Ala Ala Ala Asp Ala Arg Gly Arg Ala Gly His Arg Ser Ala Ala
35 40 45
gct tcc aac ctc tcc gcc ctc agc ctc cag gag gca cag cag att ctc 254
Ala Ser Asn Leu Ser Gly Leu Ser Leu Gln Glu Ala Gln Gln Ile Leu
15 50 55 60
aac gtg tcc aag ctg agc cct gag gag gtc cag aag aac tat gaa cac 302
Asn Val Ser Lys Leu Ser Pro Glu Glu Val Gln Lys Asn Tyr Glu His
65 70 75
tta ttt aag gtg aat gat aaa tcc gtg ggt gcc tcc ttc tac ctg cag 350
20 Leu Phe Lys Val Asn Asp Lys Ser Val Gly Gly Ser Phe Tyr Leu Gln
80 85 90 95
tca aag gtg gtc cgc gca aag gag cgc ctg gat gag gaa ctc aaa atc 398
Ser Lys Val Val Arg Ala Lys Glu Arg Leu Asp Glu Glu Leu Lys Ile
100 105 110
25 cag gcc cag gag gac aga gaa aaa ggg cag atg ccc cat acg tgactgtc 450
Gln Ala Gln Glu Asp Arg Glu Lys Gly Gln Met Pro His Thr
115 120 125
gtccccccg cccacccgc cgcctctaat ttatagcttg gtaataaatt tctttctgc 510

30 <210> 22
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35 <221> CDS

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<222> (104)...(499)

<400> 22

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                                     Met Ala Gly Ile
                                     1
aaa gct ttg att agt ttg tcc ttt gga gga gca atc gga ctg atg ttt   163
Lys Ala Leu Ile Ser Leu Ser Phe Gly Gly Ala Ile Gly Leu Met Phe
10   5           10           15           20
ttg atg ctt gga tgt gcc ctt cca ata tac aac aaa tac tgg ccc cto   211
Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys Tyr Trp Pro Leu
                                     25           30           35
ttt gtt cta ttt ttt tac atc ctt tca cct att cca tac tgc ata gca   259
15  Phe Val Leu Phe Phe Tyr Ile Leu Ser Pro Ile Pro Tyr Cys Ile Ala
                                     40           45           50
aga aga tta gtg gat gat aca gat gct atg agt aac gct tgt aag gaa   307
Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn Ala Cys Lys Glu
                                     55           60           65
20  ctt gcc atc ttt ctt aca acg ggc att gtc gtg tca gct ttt gga ctc   355
Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser Ala Phe Gly Leu
                                     70           75           80
cct att gta ttt gcc aga gca cat ctg att gag tgg gga gct tgt gca   403
Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp Gly Ala Cys Ala
25  85           90           95           100
ctt gtt ctc aca gga aac aca gtc atc ttt gca act ata cta ggc ttt   451
Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr Ile Leu Gly Phe
                                     105           110           115
ttc ttg gtc ttt gga agc aat gac gac ttc agc tgg cag cag tgg tgaa   500
30  Phe Leu Val Phe Gly Ser Asn Asp Asp Phe Ser Trp Gln Gln Trp
                                     120           125           130
aagaaattac tgaactattg tcaaatggac ttctgtcat ttgttgcca ttcacgcaca   560
caggagatgg ggcagttaat gctgaatggt atagcaagcc tcttgggggt attttaggtg   620
ctccctcttc acttttattg taagcatact attttcacag agacttgctg aaggattaaa   680
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tggtgttgag ttagttgtgg gacccggagc tctgaccca ggggtggcc caccgaaccg 120
gtgacacagc ggcagggcgtt agggctcggg agccgcgagc ctggcctcgt cctagagetc 180
ggccgagccg tcgccgccgt cgtcccccgc cccagtcag caaacccgcg ccgcgggcgc 240
15 gcccccgtc tcgctgtct ctcgatggc gtcgcctca ggggcc atg gcg aag 295
Met Ala Lys
1
cac gag cag atc ctg gtc ctc gat ccg ccc aca gac ctc aaa ttc aaa 343
His Glu Gln Ile Leu Val Leu Asp Pro Pro Thr Asp Leu Lys Phe Lys
20 5 10 15
ggc ccc ttc aca gat gta gtc act aca aat ctt aaa ttg cga aat cca 391
Gly Pro Phe Thr Asp Val Val Thr Thr Asn Leu Lys Leu Arg Asn Pro
20 25 30 35
tcg gat aga aaa gtg tgt ttc aaa gtg aag act aca gca cct cgc cgg 439
25 Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala Pro Arg Arg
40 45 50
tac tgt gtg agg ccc aac agt gga att att gac cca ggg tca act gtg 487
Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly Ser Thr Val
55 60 65
30 act gtt tca gta atg cta cag ccc ttt gac tat gat ccg aat gaa aag 535
Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro Asn Glu Lys
70 75 80
agt aaa cac aag ttt atg gta cag aca att ttt gct cca cca aac act 583
35 Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro Pro Asn Thr
85 90 95

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	tca gat atg gaa gct gtg tgg aaa gag gca aaa cct gat gaa tta atg	631
	Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp Glu Leu Met	
	100 105 110 115	
	gat tcc aaa ttg aga tgc gta ttt gaa atg ccc aat gaa aat gat aaa	679
5	Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu Asn Asp Lys	
	120 125 130	
	ttg aat gat atg gaa cct agc aaa gct gtt cca ctg aat gca tct aag	727
	Leu Asn Asp Met Glu Pro Ser Lys Ala Val Pro Leu Asn Ala Ser Lys	
	135 140 145	
10	caa gat gga cct atg cca aaa cca cac agt gtt tca ctt aat gat acc	775
	Gln Asp Gly Pro Met Pro Lys Pro His Ser Val Ser Leu Asn Asp Thr	
	150 155 160	
	gaa aca agg aaa cta atg gaa gag tgt aaa aga ctt cag gga gaa atg	823
	Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Gln Gly Glu Met	
15	165 170 175	
	atg aag cta tca gaa gaa aat cgg cac ctg aga gat gaa ggt tta agg	871
	Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu Gly Leu Arg	
	180 185 190 195	
	ctc aga aag gta gca cat tgc gat aaa oot gga tca acc tca act gca	919
20	Leu Arg Lys Val Ala His Ser Asp Lys Pro Gly Ser Thr Ser Thr Ala	
	200 205 210	
	tcc ttc aga gat aat gtc acc agt cct ctt cct tca ctt ctt gtt gta	967
	Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu Leu Val Val	
	215 220 225	
25	att gca gcc att ttc att gga ttc ttt cta ggg aaa ttc atc ttg	1012
	Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Gly Lys Phe Ile Leu	
	230 235 240	
	tagagtgaag catgcagagt gctgtttctt tttttttttt ttctcttgac cagaaaaa	1070
	gatttggtta cctaccattt cattggtagt atggcccacg gtgaccattt ttttgtgtgt	1130
30	acagcgtcat ataggctttg cctttaatga tctcttacgg tttagaaaca caataaaaac	1190
	aaactgttcg gctactggac aggttgtata ttaccagatc atcactagea gatgtcagtt	1250
	gcacattgag tcttttatga aattcataaa taaagaattg ttctttcttt gtgggtttta	1310
	taagagttca agaattgttc agagtcttgt aaatgttatt ttaataatcc ctttaaattt	1370
	tatctgttgc tgttacctct tgaaatatga tttatttaga ttgctaatac cactcattca	1430
35	ggaaatgcca agaggtattc cttggggaaa tgggtcctct tacagtgtaa atttttctc	1490

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ctttaccttt gctaataatca tggcagaatt tttcttatec cttgtgaggc agttgttgac 1550
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ttaacagat 1619

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  <222> (65)...(859)

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15 gacc atg ttc gtt ccc tgc ggg gag tgc gcc ccc gac ctt gcc ggc ttc 109
    Met Phe Val Pro Cys Gly Glu Ser Ala Pro Asp Leu Ala Gly Phe
      1         5         10        15
acc ctc cta atg cca gca gta tct gtt gga aat gtt gcc cag ctt gca 157
Thr Leu Leu Met Pro Ala Val Ser Val Gly Asn Val Gly Gln Leu Ala
20          20          25          30
atg gat ctg att att tct aca ctg aat atg tct aag att ggt tac ttc 205
Met Asp Leu Ile Ile Ser Thr Leu Asn Met Ser Lys Ile Gly Tyr Phe
      35          40          45
tat acc gat tgt ctt gtg cca atg gtt gga aac aat cca tat gcg acc 253
25 Tyr Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr
      50          55          60
aca gaa gga aat tca aca gaa ctt agc ata aat gct gaa gtg tat tca 301
Thr Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser
      65          70          75
ttg cct tca aga aag ctg gtg gct cta cag tta aga tcc att ttt att 349
30 Leu Pro Ser Arg Lys Leu Val Ala Leu Gln Leu Arg Ser Ile Phe Ile
      80          85          90          95
aag tat aaa tca aag cca ttc tgt gaa aaa ctg ctt tcc tgg gtg aaa 397
Lys Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys
35          100          105          110

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	ago agt ggc tgt gcc aga gtc att gtt ctt tcg agc agt cat tca tat	445
	Ser Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr	
	115 120 125	
	cag cgt aat gat ctg cag ctt cgt agt act ccc ttc cgg tac cta ctt	493
5	Gln Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu	
	130 135 140	
	aca cct tcc atg caa aaa agt gtt caa aat aaa ata aag agc ctt aac	541
	Thr Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn	
	145 150 155	
10	tggt gaa gaa atg gaa aaa agc cgg tgc att cct gaa ata gat gat tcc	589
	Trp Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser	
	160 165 170 175	
	gag ttt tgt atc cgc att cgg gga gga ggt atc aca aaa aca ctc tat	637
	Glu Phe Cys Ile Arg Ile Pro Gly Gly Gly Ile Thr Lys Thr Leu Tyr	
15	180 185 190	
	gat gaa agc tgt tct aaa gaa atc caa atg gca gtt ctg ctg aaa ttt	685
	Asp Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe	
	195 200 205	
	gtt tca gaa ggg gac aac atc cca gat gca tta ggt ctt gtt gag tat	733
20	Val Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr	
	210 215 220	
	ctt aat gag tgg ctt cag ata ctc aaa cca ctt agc gat gac ccc aca	781
	Leu Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr	
	225 230 235	
25	gta tct gcc tca cgg tgg aaa ata cca agt tct tgg aga tta ctc ttt	829
	Val Ser Ala Ser Arg Trp Lys Ile Pro Ser Ser Trp Arg Leu Leu Phe	
	240 245 250 255	
	ggc agt ggt ctt ccc cct gca ctt ttc tgatctaatt tctgttttat acct	880
	Gly Ser Gly Leu Pro Pro Ala Leu Phe	
30	260	
	tatacccaaa acacttacta ccaacacagc tgtaaaccat totatacaaa aaaattgtat	940
	gatctgggtat taggaaatta ctttcacagt aaatatcaaa gaaaaaagat taagggtctc	1000
	tttgccatgc ttttcatcat atgcaccaaa tgtaaatttt gtacaataaa attttatctc	1060
	ctaagt	1066
35		

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	1	
	ggg tct cgg ttg tcc cag cct ttt gag tcc tat atc act gcg cct ccc	104
	Gly Ser Arg Leu Ser Gln Pro Phe Glu Ser Tyr Ile Thr Ala Pro Pro	
15	5 10 15	
	ggg acc gcc gcc gcg ccc gcc aaa cct gcg ccc cca gct aca ccc gga	152
	Gly Thr Ala Ala Ala Pro Ala Lys Pro Ala Pro Pro Ala Thr Pro Gly	
	20 25 30	
	gcg ccg acc tcc cca gca gaa cac cgc ctg ttg aag acc tgc tgg agc	200
20	Ala Pro Thr Ser Pro Ala Glu His Arg Leu Leu Lys Thr Cys Trp Ser	
	35 40 45	
	tgt cgc gtg ctt tct ggg ttg ggg ctg atg ggg gcg gcc ggg tac gtg	248
	Cys Arg Val Leu Ser Gly Leu Gly Leu Met Gly Ala Gly Gly Tyr Val	
	50 55 60 65	
25	tac tgg gtg gca cgg aag ccc atg aag atg gga tac ccc ccg agt cca	296
	Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser Pro	
	70 75 80	
	tgg acc att acg cag atg gtc atc gcc ctc agc att gcc acc tgg ggt	344
	Trp Thr Ile Thr Gln Met Val Ile Gly Leu Ser Ile Ala Thr Trp Gly	
30	85 90 95	
	atc gtt gtc atg gca gac ccc aaa ggg aag gcc tac cgc gtt gtt t	390
	Ile Val Val Met Ala Asp Pro Lys Gly Lys Ala Tyr Arg Val Val	
	100 105 110	
	gaaagtacca ccagtgaaatc tgtttctgtg ctctgtccct ttcccgtga cacacacagc	450
35	agggcatggaa ttttaatgggt gttctggaca gacacttgta catggacaga catacaact	510

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gtggatacta caagaactgag aagaaaatcg tatgttgta ttctctgggt atggagtgtt 570
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5 <211> 1021
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15 ggtgagcggg cgctagggcc gcgagccccc gccggccctt cctccagcgc cctgcggacc 180
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cctggaacct ctgggagggc tgcagagtaa gtccgcctc tgcgtccga cggaggcacc 360
aggcctgtgg agtaggtccc tctgttccga caggtgcgac acctggcget cc atg ctt 418
20 Met Leu
1
gcg ggt gcc ggg agg cct ggc ctc ccc cag ggc cgc cac ctc tgc tgg 466
Ala Gly Ala Gly Arg Pro Gly Leu Pro Gln Gly Arg His Leu Cys Trp
5 10 15
25 ttg ctc tgt gct ttc acc tta aag ctc tgc caa gca gag gct ccc gtg 514
Leu Leu Cys Ala Phe Thr Leu Lys Leu Cys Gln Ala Glu Ala Pro Val
20 25 30
cag gaa gag aag ctg tca gca agc acc tca aat ttg cca tgc tgg ctg 562
Gln Glu Glu Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys Trp Leu
30 35 40 45 50
gtg gaa gag ttt gtg gta gca gaa gag tgc tct cca tgc tct aat ttc 610
Val Glu Glu Phe Val Val Ala Glu Glu Cys Ser Pro Cys Ser Asn Phe
55 60 65
cgg gct aaa act acc cct gag tgt ggt ccc aca gga tat gta gag aaa 658
35 Arg Ala Lys Thr Thr Pro Glu Cys Gly Pro Thr Gly Tyr Val Glu Lys

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	70	75	80	
	atc aca tgc agc tca tct aag aga aat gag ttc aaa agc tgc cgc tca			706
	Ile Thr Cys Ser Ser Ser Lys Arg Asn Glu Phe Lys Ser Cys Arg Ser			
	85	90	95	
5	gct ttg atg gaa caa cgc tta ttt tgg aag ttc gaa ggg gct gtc gtg			754
	Ala Leu Met Glu Gln Arg Leu Phe Trp Lys Phe Glu Gly Ala Val Val			
	100	105	110	
	tgt gtg gcc ctg atc ttc gct tgt ctt gtc atc att cgt cag cga caa			802
	Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln Arg Gln			
10	115	120	125	130
	ttg gac aga aag gct ctg gaa aag gtc cgg aag caa atc gag tcc ata			850
	Leu Asp Arg Lys Ala Leu Glu Lys Val Arg Lys Gln Ile Glu Ser Ile			
	135	140	145	
	tagctacatt ccacccttgt atcctgggtc ttgagaccc tatctcagac agtgaaagt			910
15	aaatggactg atttgactc ttggttcttt ggagccttgt ggtggaatcc cctttccccc			970
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	<211> 1432			
20	<212> DNA			
	<213> Homo sapiens			
	<220>			
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	<222> (331)...(1365)			
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	gcccagctcc gggggcgccc cgggtgcccc tccgagcctg ctgcactcca cgtccccta			120
	ccagggtccc agcccccagg gaaatctccg accaggcccc cccaggagcc agatccaggc			180
30	tcctggaaga accatgtccg gcagctactg gtcattgccag gcacacactg ctgcccaga			240
	ggagctgtg tttgaattat ctgtgaatgt tgggaagagg aatgccagag ctgcggctg			300
	aaaattaccc aaccaagaga aatctgcagg atg gac ttt ctg gtc etc ttc ttg			354
	Met Asp Phe Leu Val Leu Phe Leu			
	1	5		
35	ttc tac ctg gct tcc gtg ctg atg ggt ctt gtt ctt atc tgc gtc tgc			402

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	Phe Tyr Leu Ala Ser Val Leu Met Gly Leu Val Leu Ile Cys Val Cys	
	10 15 20	
	tcg aaa acc cat agc ttg aaa ggc ctg gcc agg gga gga gca cag ata	450
	Ser Lys Thr His Ser Leu Lys Gly Leu Ala Arg Gly Gly Ala Gln Ile	
5	25 30 35 40	
	ttt tcc tgt ata att cca gaa tgt ctt cag aga gcc gtg cat gga ttg	498
	Phe Ser Cys Ile Ile Pro Glu Cys Leu Gln Arg Ala Val His Gly Leu	
	45 50 55	
	ctt cat tac ctt ttc cat acg aga aac cac acc ttc att gtc ctg cac	546
10	Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe Ile Val Leu His	
	60 65 70	
	ctg gtc ttg cca ggg atg gtt tat act gag tac acc tgg gaa gta ttt	594
	Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr Trp Glu Val Phe	
	75 80 85	
15	ggc tac tgt cag gag ctg gag ttg tcc ttg cat tac ctt ctt ctg ccc	642
	Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr Leu Leu Leu Pro	
	90 95 100	
	tat ctg ctg cta ggt gta aac ctg ttt ttt ttc acc ctg act tgt gga	690
	Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Phe Thr Leu Thr Cys Gly	
20	105 110 115 120	
	acc aat cct ggc att ata aca aaa gca aat gaa tta tta ttt ctt cat	738
	Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu Leu Phe Leu His	
	125 130 135	
	gtt tat gaa ttt gat gaa gtg atg ttt cca aag aac gtg agg tgc tct	786
25	Val Tyr Glu Phe Asp Glu Val Met Phe Pro Lys Asn Val Arg Cys Ser	
	140 145 150	
	act tgt gat tta agg aaa cca gct cga tcc aag cac tgc agt gtg tgt	834
	Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Lys His Cys Ser Val Cys	
	155 160 165	
30	aac tgg tgt gtg cac cgt ttc gac cat cac tgt gtt tgg gtg aac aac	882
	Asn Trp Cys Val His Arg Phe Asp His His Cys Val Trp Val Asn Asn	
	170 175 180	
	tgc atc ggg gcc tgg aac atc agg tac ttc ctc atc tac gtc ttg acc	930
	Cys Ile Gly Ala Trp Asn Ile Arg Tyr Phe Leu Ile Tyr Val Leu Thr	
35	185 190 195 200	

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ttg acg gcc tag gct gcc acc gtc gcc att gtg agc acc act ttt ctg 978
 Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser Thr Thr Phe Leu
 205 210 215
 gtc cac ttg gtg gtg atg tca gat tta tac cag gag act tac atc gat 1026
 5 Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu Thr Tyr Ile Asp
 220 225 230
 gac ett gga cac ctc cat gtt atg gac acg gtc ttt ett att cag tac 1074
 Asp Leu Gly His Leu His Val Met Asp Thr Val Phe Leu Ile Gln Tyr
 235 240 245
 10 ctg ttc ctg act ttt cca egg att gtc ttc atg ctg ggc ttt gtc gtg 1122
 Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu Gly Phe Val Val
 250 255 260
 GTT CTG AGC TTC CTC CTG GGT GGC TAC CTG TTG TTT GTC CTG TAT CTG 1170
 Val Leu Ser Phe Leu Leu Gly Gly Tyr Leu Leu Phe Val Leu Tyr Leu
 15 265 270 275 280
 gcg gcc acc aac cag act act aac gag tgg tac aga ggt gac tgg gcc 1218
 Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg Gly Asp Trp Ala
 285 290 295
 tgg tgc cag cgt tgt ccc ett gtg gcc tgg cct cgg tca gca gag ccc 1266
 20 Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro Ser Ala Glu Pro
 300 305 310
 caa gtc cac cgg aac att cac tcc cat ggg ett cgg agc aac ett caa 1314
 Gln Val His Arg Asn Ile His Ser His Gly Leu Arg Ser Asn Leu Gln
 315 320 325
 25 gag atc ttt cta cct gcc ttt cca tgt cat gag agg aag aaa caa gaa 1362
 Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg Lys Lys Gln Glu
 330 335 340
 tgacaagtgt atgactgcct ttgagctgta gtcccggttt atttacacat gtggatcc 1420
 tcgttttcca ag 1432
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 <211> 601
 <212> DNA
 <213> Homo sapiens
 35 <220>

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<221> CDS

<222> (62)...(355)

<400> 28

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   c atg act aaa aag aag cgg gag aat ctg ggc gtc gct cta gag atc gat      109
     Met Thr Lys Lys Lys Arg Glu Asn Leu Gly Val Ala Leu Glu Ile Asp
       1         5         10        15
10  ggg cta gag gag aag ctg tcc cag tgt cgg aga gac ctg gag gcc gtg      157
     Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val
       20        25        30
     aac tcc aga ctc cac agc cgg gag ctg agc cca gag gcc agg agg tcc      205
     Asn Ser Arg Leu His Ser Arg Glu Leu Ser Pro Glu Ala Arg Arg Ser
       35        40        45
15  ctg gag aag gag aaa aac agc cta atg aac aaa gcc tcc aac tac gag      253
     Leu Glu Lys Glu Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Glu
       50        55        60
     aag gaa ctg aag ttt ctt cgg caa gag aac cgg aag aac atg ctg ctc      301
     Lys Glu Leu Lys Phe Leu Arg Gln Glu Asn Arg Lys Asn Met Leu Leu
20  65          70          75          80
     tct gtg gcc atc ttt atc ctc ctg acg ctc gtc tat gcc tac tgg acc      349
     Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr
       85        90        95
25  atg tgagcctggc acttccccac aaccagcaca ggcttccact tggccccc      400
     Met

     tgatcaggat caagcaggca cttcaagcct caataggacc aaggtgctgg ggtgtcccc      460
     tcccaacctc gtgttaagc atggcttccct ggcggccag gccttgctc cctggcctgc      520
     tgggggggtc cgggtctcca gaaggacatg gtgctggtec ctcccttagc ccaagggaga      580
30  ggcaataaag acacaaagct g      601

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<210> 29

<211> 585

<212> DNA

35 <213> Homo sapiens

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<220>

<221> CDS

<222> (78)...(452)

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 gcagagtoag taagacc atg gct aag tcc tcg atg tct aag ggt tgc ttt 110
 Met Ala Thr Ser Ser Met Ser Lys Gly Cys Phe
 1 5 10

10 gtt ttt aag cca aac tcc aaa aag aga aag atc tct ctg cca ata gag 158
 Val Phe Lys Pro Asn Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Glu
 15 20 25
 gac tat ttt aac aaa ggg aaa aat gag cct gag gac agt aag ctt cga 206
 Asp Tyr Phe Asn Lys Gly Lys Asn Glu Pro Glu Asp Ser Lys Leu Arg
 15 30 35 40
 ttc gaa act tat cag ttg ata tgg cag cag atg aaa tct gaa aat gag 254
 Phe Glu Thr Tyr Gln Leu Ile Trp Gln Gln Met Lys Ser Glu Asn Glu
 45 50 55
 cga cta caa gag gaa tta aat aaa aac ttg ttt gac aat ctg att gaa 302
 Arg Leu Gln Glu Glu Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Glu
 20 60 65 70 75
 ttt ctg caa aaa tca cat tct gga ttc cag aag aat tca aga gac ttg 350
 Phe Leu Gln Lys Ser His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu
 80 85 90

25 ggc ggt caa ata aaa ctc aga gaa att cca act gct gct ctt gtt ctt 398
 Gly Gly Gln Ile Lys Leu Arg Glu Ile Pro Thr Ala Ala Leu Val Leu
 95 100 105
 ggt ata tat gcg tat gtt tgt tca tgc atg cat ctc tgt gta ttt cgt 446
 Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg
 30 110 115 120
 ttt taaattttt tttattgttg agaatagtgg aaggaccrgt tttgatgagc c 500
 Phe

tattttgtct ctcttatttg taacaattaaa ccaactatag tttatattac atattttcaa 560
 35 aaaccaataa aaattcctta tcttt 585

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<211> 1100
<212> DNA
5  <213> Homo sapiens
    <220>
    <221> CDS
    <222> (57)...(1040)

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                                           Met
                                           1

    gcc gag ctc ccc ggg ccc ttt ctc tgc ggg gcc ctg cta ggc ttc ctg      107
15  Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly Phe Leu
        5             10             15
    tgc ctg agt ggg ctg gcc gtg gag gtg aag gta ccc aca gag ccc ctg      155
    Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro Leu
        20             25             30
20  agc acg ccc ctg ggg aag aca gcc gag ctg acc tgc acc tac agc acg      203
    Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser Thr
        35             40             45
    tcg gtg gga gac agc ttc gcc ctg gag tgg agc ttt gtg cag cct ggg      251
    Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro Gly
25  50             55             60             65
    aaa ccc atc tct gag tcc cat cca atc ctg tac ttc acc aat ggc cat      299
    Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly His
        70             75             80
    ctg tat cca act ggt tct aag tca aag cgg gtc agc ctg ctt cag aac      347
30  Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln Asn
        85             90             95
    ccc ccc aca gtg ggg gtg gcc aca ctg aaa ctg act gac gtc cac ccc      395
    Pro Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His Pro
        100            105            110
35  tca gat act gga acc tac ctc tgc caa gtc aac aac cca cca gat ttc      443

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	Ser Asp Thr Gly Thr Tyr Leu Cys Gln Val Asn Asn Pro Pro Asp Phe	
	115 120 125	
	tac acc aat ggg ttg ggg cta atc aac ctt act gtg ctg gtt ccc ccc	491
	Tyr Thr Asn Gly Leu Gly Leu Ile Asn Leu Thr Val Leu Val Pro Pro	
5	130 135 140 145	
	agt aat ccc tta tgc agt cag agt gga caa acc tct gtg gga ggc tct	539
	Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly Ser	
	150 155 160	
	act gca ctg aga tgc agc tct tcc gag ggg gct cct aag cca gtg tac	587
10	Thr Ala Leu Arg Cys Ser Ser Ser Glu Gly Ala Pro Lys Pro Val Tyr	
	165 170 175	
	aac tgg gtg cgt ctt gga act ttt cct aca cct tct cct ggc agc atg	635
	Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser Met	
	180 185 190	
15	gtt caa gat gag gtg tct ggc cag ctc att ctc acc aac ctc tcc ctg	683
	Val Gln Asp Glu Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser Leu	
	195 200 205	
	acc tcc tgg ggc acc tac cgc tgt gtg gcc acc aac cag atg ggc agt	731
	Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly Ser	
20	210 215 220 225	
	gca tcc tgt gag ctg acc ctc tct gtg acc gaa ccc tcc caa ggc cga	779
	Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly Arg	
	230 235 240	
	gtg gcc gga gct ctg att ggg gtg ctc ctg ggc gtg ctg ttg ctg tca	827
25	Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Leu Ser	
	245 250 255	
	gtt gct ggc ttc tgc ctg gtc agg ttc cag aaa gag agg ggg aag aag	875
	Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg Gly Lys Lys	
	260 265 270	
30	ccc aag gag aca tat ggg ggt agt gac ctt cgg gag gat gcc atc gct	923
	Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile Ala	
	275 280 285	
	cct ggg atc tct gag cac act tgt atg agg gct gat tct agc aag ggg	971
	Pro Gly Ile Ser Glu His Thr Cys Met Arg Ala Asp Ser Ser Lys Gly	
35	290 295 300 305	

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ttc ctg gaa aga ccc tgc tct gcc agc acc gtg acg acc acc aag tcc      1019
Phe Leu Glu Arg Pro Ser Ser Ala Ser Thr Val Thr Thr Thr Lys Ser
          310          315          320
aag ctc cct atg gtc gtg tgactctcc cgatccctga gggcggtag ggg      1070
5 Lys Leu Pro Met Val Val
          325
gaatatcaat aattaaagtc tgtgggtacc      1100

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    <213> Homo sapiens

<400> 31
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Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser
          20          25          30
Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys
20          35          40          45
Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val
    50          55          60
Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr
    65          70          75          80
25 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val
          85          90          95
Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu
          100          105          110
Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala
30          115          120          125
Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala
          130          135          140
Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His
    145          150          155          160
35 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu

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165 170 175
 Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val
 180 185 190
 Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro
 5 195 200 205
 Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser
 210 215 220
 Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val
 225 230 235 240
 10 Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val
 245 250 255
 Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe
 260 265 270
 Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp
 15 275 280 285
 Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr
 290 295 300
 Glu Ala Ala Val Leu Leu Phe Tyr Arg
 305 310
 20
 <210> 32
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 <212> PRT
 <213> Homo sapiens
 25
 <400> 32
 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala
 1 5 10 15
 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu
 30 20 25 30
 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe
 35 40 45
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val
 50 55 60
 35 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

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65 70 75 80
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr
 85 90 95
 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe
 5 100 105 110
 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn
 115 120 125
 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr
 130 135 140
 10 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile
 145 150 155 160
 Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu
 165 170 175
 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe
 15 180 185 190
 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val
 195 200 205
 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys
 210 215 220
 20 Arg Lys Ser Arg Thr
 225

 <210> 33
 <211> 467
 25 <212> PRT
 <213> Homo sapiens

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 30 1 5 10 15
 Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr
 20 25 30
 Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala
 35 40 45
 35 Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe

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	50	55	60
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Glu Lys		
	65	70	75 80
5	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro		
	85	90	95
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe		
	100	105	110
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr		
	115	120	125
10	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser		
	130	135	140
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp		
	145	150	155 160
	Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg		
15	165	170	175
	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu		
	180	185	190
	Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys		
	195	200	205
20	Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val		
	210	215	220
	Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser		
	225	230	235 240
	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr		
25	245	250	255
	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly		
	260	265	270
	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro		
	275	280	285
30	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr		
	290	295	300
	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val		
	305	310	315 320
	Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn		
35	325	330	335

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Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg
 340 345 350
 Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr
 355 360 365
 5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val
 370 375 380
 Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu
 385 390 395 400
 Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile
 10 405 410 415
 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn
 420 425 430
 Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu
 435 440 445
 15 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr
 450 455 460
 Asn Val Ile
 465
 20 <210> 34
 <211> 99
 <212> PRT
 <213> Homo sapiens
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 1 5 10 15
 Val Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu
 20 25 30
 30 Val Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro
 35 40 45
 Glu Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr
 50 55 60
 Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu
 35 65 70 75 80

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Phe Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys
 85 90 95
 Glu Val Leu

5 <210> 35
 <211> 189
 <212> PRT
 <213> Homo sapiens

10 <400> 35
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 1 5 10 15
 Leu Val Leu Ser Gly Ala Trp Gly Met Gln Met Trp Val Thr Phe Val
 20 25 30

15 Ser Gly Phe Leu Leu Phe Arg Ser Leu Pro Arg His Thr Phe Gly Leu
 35 40 45
 Val Gln Ser Lys Leu Phe Pro Phe Tyr Phe His Ile Ser Met Gly Cys
 50 55 60
 Ala Phe Ile Asn Leu Cys Ile Leu Ala Ser Gln His Ala Trp Ala Gln

20 65 70 75 80
 Leu Thr Phe Trp Glu Ala Ser Gln Leu Tyr Leu Leu Phe Leu Ser Leu
 85 90 95
 Thr Leu Ala Thr Val Asn Ala Arg Trp Leu Glu Pro Arg Thr Thr Ala
 100 105 110

25 Ala Met Trp Ala Leu Gln Thr Val Glu Lys Glu Arg Gly Leu Gly Gly
 115 120 125
 Glu Val Pro Gly Ser His Gln Gly Pro Asp Pro Tyr Arg Gln Leu Arg
 130 135 140
 Glu Lys Asp Pro Lys Tyr Ser Ala Leu Arg Gln Asn Phe Phe Arg Tyr

30 145 150 155 160
 His Gly Leu Ser Ser Leu Cys Asn Leu Gly Cys Val Leu Ser Asn Gly
 165 170 175
 Leu Cys Leu Ala Gly Leu Ala Leu Glu Ile Arg Ser Leu
 180 185

35

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<210> 36
 <211> 363
 <212> PRT
 <213> Homo sapiens

5

<400> 36

Met Val Asp Ser Leu Leu Ala Val Thr Leu Ala Gly Asn Leu Gly Leu
 1 5 10 15
 Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr
 20 25 30
 Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu
 35 40 45
 Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu
 50 55 60
 Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Glu Pro Arg
 65 70 75 80
 Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala
 85 90 95
 Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala
 100 105 110
 Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val
 115 120 125
 Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Gln Cys Met Ser
 130 135 140
 Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr
 145 150 155 160
 Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly
 165 170 175
 Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly
 180 185 190
 Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp
 195 200 205
 Phe Thr Arg Cys Ala Ala Asn Met Arg Ser Met Gln Arg Tyr His Gln
 210 215 220
 Asp Thr Gln Gly Trp Gly Asp Ile Gly Tyr Ser Phe Val Val Gly Ser

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225 230 235 240
 Asp Gly Tyr Val Tyr Glu Gly Arg Gly Trp His Trp Val Gly Ala His
 245 250 255
 Thr Leu Gly His Asn Ser Arg Gly Phe Gly Val Ala Ile Val Gly Asn
 5 260 265 270
 Tyr Thr Ala Ala Leu Pro Thr Glu Ala Ala Leu Arg Thr Val Arg Asp
 275 280 285
 Thr Leu Pro Ser Cys Ala Val Arg Ala Gly Leu Leu Arg Pro Asp Tyr
 290 295 300
 10 305 310 315 320
 Ala Leu Phe Asp Leu Leu Arg Thr Trp Pro His Phe Thr Ala Thr Val
 325 330 335
 Lys Pro Arg Pro Ala Arg Ser Val Ser Lys Arg Ser Arg Arg Glu Pro
 15 340 345 350
 Pro Pro Arg Thr Leu Pro Ala Thr Asp Leu Gln
 355 360

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 <212> PRT
 <213> Homo sapiens

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 Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr Arg Gly Arg Arg
 20 25 30
 Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys Ser Ala Glu Asp
 30 35 40 45
 Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala Glu Gln Leu Gln
 50 55 60
 Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro Val Ile Ile Glu
 65 70 75 80
 35 Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe Ser Val Asn Gln

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	85	90	95
	Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val Ala Asn Lys Ile		
	100	105	110
	Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu Asn Ala Leu Asn		
5	115	120	125
	Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile Lys Val Gln Val		
	130	135	140
	Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala Met Thr Glu Gly		
	145	150	155
10	Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser Leu Tyr Asp Ser		
	165	170	175
	His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr Leu Phe Gln Asn		
	180	185	190
	Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala Val Gln Pro Thr		
15	195	200	205
	Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly Glu Glu Cys Ala		
	210	215	220
	Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala Glu Val Lys Glu		
	225	230	235
20	Lys Val Val Thr Ile Ile Pro Lys Ile		
	245		
	<210> 38		
	<211> 98		
25	<212> PRT		
	<213> Homo sapiens		
	<400> 38		
	Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile		
30	1	5	10
	Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe		
	20	25	30
	Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu		
	35	40	45
35	Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln		

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50 55 60
 Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly
 65 70 75 80
 Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met
 5 85 90 95
 Val Arg

 <210> 39
 <211> 172
 10 <212> PRT
 <213> Homo sapiens

 <400> 39
 Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu
 15 1 5 10 15
 Ala Leu Val Leu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly
 20 20 25 30
 Gln Thr Pro Arg Pro Ala Glu Arg Gly Pro Pro Val Arg Leu Phe Thr
 35 40 45
 20 Glu Glu Glu Leu Ala Arg Tyr Gly Gly Glu Glu Glu Asp Gln Pro Ile
 50 55 60
 Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu
 65 70 75 80
 Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser
 25 85 90 95
 Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His
 100 105 110
 Asp Thr Thr Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Glu Val
 115 120 125
 30 Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala
 130 135 140
 Arg Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro
 145 150 155 160
 Glu Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe
 35 165 170

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<210> 40
 <211> 120
 <212> PRT
 5 <213> Homo sapiens

 <400> 40
 Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser Ser Lys
 1 5 10 15
 10 Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile Asp Leu
 20 25 30
 Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile Ala Leu
 35 40 45
 Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile Gly Ser
 15 50 55 60
 Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg Ala Val
 65 70 75 80
 Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe Tyr His
 85 90 95
 20 Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr Ser Tyr
 100 105 110
 Asp Asp Ile Pro Asp Phe Asp Asp
 115 120

 25 <210> 41
 <211> 939
 <212> DNA
 <213> Homo sapiens

 30 <400> 41
 atgaaccaac tcagcttccg gctgtttctc atagcgacca ccagaggatg gactacagat 60
 gaggetaata cttaactcaa ggaatggacc tgtttctctg ctccatctct gccagaagc 120
 tgcaaggaaa tcaagacga atgtcctagt gcatttgatg gcctgtatct tctccgcact 180
 gagaatggtg ttatctacca gaccttctgt gacatgacct ctgggggtgg cggtggacc 240
 35 ctggtggcca gcgtgcata gaatgacatg cgtgggaagt gcacgggtgg cgatcgtctg 300

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tccagtcagc agggcagcaa agcagactac ccagaggggg acggcaactg ggccaactac 360
 aacacctttg gatctgcaga ggcggccacg agcgtgact acaagaaccc tggctactac 420
 gacatccagg ccaaggacct gggcatctgg cacgtgcca ataagteccc catgcagcac 480
 tggagaaaca gctccctgct gaggtaccgc acggacactg gcttctcca gacactggga 540
 5 cataatctgt ttggcatcta ccagaaatat ccagtgaat atggagaagg aaagtgttg 600
 actgacaacg gcccggtgat cctgtggtc tatgatttg gcgacgcca gaaaaagca 660
 tcttattact caccstatgg ccagcgggaa ttcactgagg gatttgttca gttcagggtg 720
 tttataacg agagagcagc caacgccttg tgtgtggaa tgagggtcac cggatgtaac 780
 actgagcacc actgcattgg tggaggagga tactttccag aggccagtcc ccagcagtgt 840
 10 ggagattttt ctggtttga ttggagtga tatggaactc atgttggtta cagcagcagc 900
 cgtgagataa ctgaggcagc tgtgetteta ttctatcgt 939

<210> 42

<211> 687

15 <212> DNA

<213> Homo sapiens

<400> 42

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 20 ctgctgcctg gggcggcggg cttcacacct tccctcgata ggcacttcac ctttaacctt 120
 cccgcgggco agaaggagtg cttctaccag cccatgccc tgaaggctc gctggagatc 180
 gagtaccaag ttttagatgg agcaggatta gatattgatt tccatcttgc ctctccagaa 240
 ggcaaaacct tagttttga acaagaaaa tcagatggag ttcacactgt agagactgaa 300
 gttggtgatt acatgttttg ctttgacaat acattcagca ccatttttga gaaggtgatt 360
 25 ttctttgaat taactctgga taatatggga gaacaggcac aagaacaaga agattggaag 420
 aaatatatta ctggcacaga tatattgat atgaaactgg aagacatcct ggaatccatc 480
 aacagcaca agtcagact aagcaaaagt gggcacatac aaattctgct tagagcattt 540
 gaagctcgtg atcgaaacat acaagaaagc aactttgata gagtcaattt ctggtctatg 600
 gtttaatttag tggatcgtgt ggtggtgtca gccattcaag tttatatgct gaagagtctg 660
 30 tttgaagata agaggaaaag tagaact 687

<210> 43

<211> 1401

<212> DNA

35 <213> Homo sapiens

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<400> 43

	atgcggcccc aggagctccc caggctcgcg tccccgtgc tgcgtttgct gttgctgctg	60
	ctgccgcgcg cgccgtgccc tgcccacagc gccacgcgct tcgaccccac ctgggagctc	120
5	ctggacgccc gccagctgcc cgcgtgggtt gaccaggcca agttcggcat ctccatccac	180
	tggggagtgt tttccgtgcc cagcttcggt agcagtggtt tctggtggta ttggcaaaag	240
	gaaaagatac cgaagtatgt ggaatttatg aaagataatt acctcctag tttcaaatat	300
	gaagattttg gaccactatt tacagcaaaa ttttttaatg ccaaccagtg ggcagatatt	360
	tttcaggcct ctggtgccaa atacattgtc ttaacttcca aacatcatga aggcctttacc	420
10	tttgtgggggt cagaatatto gtggaactgg aatgccatag atgagggggc caagagggac	480
	attgtcaagg aacttgaggt agccattagg aacagaactg acctgcgttt tggactgtac	540
	tattcccttt ttgaatgggt tcatccgctc ttccttyagg atgaatccag ttcattccat	600
	aagcggcaat ttccagtctc taagacattg ccagagctct atgagttagt gaacaactat	660
	cagcctgagg ttctgtggtc ggtggtgac ggaggagcac cggatcaata ctggaaacagc	720
15	acaggcttct tggcctgggt atataatgaa agcccagttc ggggcacagt agtcaccaat	780
	gacgtttggg gagctggtag catctgtaag catggtggct tctataacctg cagtgatcgt	840
	tataaccacg gacatctttt gccacataaa tgggaaaact gcatgacaat agacaactcg	900
	tcttggggct ataggaggga agctggaatc tctgactatc ttacaattga agaattgggtg	960
	aagcaacttg tagagacagt ttcattgtga ggaatcttt tgaatgaat tggggccaca	1020
20	ctagatggca ccatttctgt agtttttgag gagcgactga ggcaaatggg gtccctggta	1080
	aaagtcaatg gagaagctat ttatgaaacc catacctggc gatcccagaa tgacactgtc	1140
	accccagatg tgtggtacac atccaagcct aaagaaaaat tagtctatgc cttttttctt	1200
	aaatggccca catcaggaca gctgttcctt ggccatccca aagctattct gggggcaaca	1260
	gaggtgaaac tactggggca tggaaagoca cttaactgga tttcttttga gcaaaatggc	1320
25	attatggtag aactgccaca gctaacatt catcagatgc cgtgtaaatg gggctgggct	1380
	ctagccctga ctaatgtgat c	1401

<210> 44

<211> 297

30 <212> DNA

<213> Homo sapiens

<400> 44

	atggataacg tgcagccgaa aataaaacat cgcctcttct gcttcagtgt gaaaggccac	60
35	gtgaagatgc tgcggctgga tattatcaac tcaactggta caacagtatt catgctcacc	120

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		gtatctgtgt tggcactgat accagaaacc acaacattga cagttggtgg aggggtgtt	180
		gcacttgtga cagcagtatg ctgtcttgcc gacggggccc ttatttaccg gaagcttctg	240
		ttcaatccca ggggtcctta ccagcaaaag cctgtgcatg aaaaaaaga agttttg	297
5	<210>	45	
	<211>	567	
	<212>	DNA	
	<213>	Homo sapiens	
10	<400>	45	
		atggaggaag gcgggaacct aggaggcctg attaagatgg tccatctact ggtcttgtca	60
		gggtgctggg gcattgcaaat gtyggtgacc ttcgtctcag gcttcctgot ttccogaagc	120
		cttcccgac ataccttcgg actagtgcag agcaaaactct tcccttcta ctccacatc	180
		tccatgggt gtgccttcat caacctctgc atcttggctt caccagatgc ttgggtcag	240
15		ctcacattct gggaggccag ccagctttac ctgctgttcc tgagccttac gctggcact	300
		gtcaacgccc gctggctgga accccgcacc acagctgcca tgtgggccct gcaaacctg	360
		gagaaggagc gaggcctggg tggggaggta ccaggcagcc accagggctc cgatccctac	420
		cgccagctgc gagagaagga ccccaagtac agtgcctccc gccagaattt ctcccgctac	480
		catgggtgt cctctctttg caatctgggc tgcgtcctga gcaatgggt ctgtctcgt	540
20		ggccttgcgc tggaaataag ggcctc	567
	<210>	46	
	<211>	1089	
	<212>	DNA	
25	<213>	Homo sapiens	
	<400>	46	
		atgggtggaca gctcctggc agtcacctg gctggaaacc tgggcctgac cttectccga	60
		ggttcccaga ccagagcca tccagaactg ggaactgagg gctgctggga ccagctctct	120
30		gcccctcgga cctttacgt ttggacccc aaggcatctc tgttaaccaa ggccttctc	180
		aatggcgccc tggatgggt cctccttggg gactacctga gccggactcc tgagcccggy	240
		ccatccctca gccacttgc gagccagtac tatggggctg ggggtggccag agaccaggy	300
		ttccgcagca acttccgacg gcagaacggt gctgctctga ctccagctc cctcctggcc	360
		cagcaggtgt ggggaacct tgtccttcta cagaggtgg agccagtaca cctccagctt	420
35		cagtgcctga gccaaagaca gctggcccag gtggctgcca atgctaccaa ggaattcact	480

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gaggccttcc tgggatgcc ggccatccac ccccgctgcc gctggggagc ggcgccttat 540
 cggggcgccc cgaagctgct gcagctgccg ctgggattct tgtacgtgca tcacacctac 600
 gtgctctgac caccctgcac ggacttcacg cgtgctgag ccaacatgcy ctccatgcag 660
 cgtaccaccc aggcacgcga aggctgggga gacatcggct acagtctcgt ggtgggctcg 720
 5 gacggctacg tgtacgaggg acgcggctgg cactgggtgg ggcgccacac gctcgggcac 780
 aactccgggg gcttcggcgt ggccatagtg ggcaactaca ccgcggcgct gccaccgcag 840
 gccgctctgc gcacggtgcy cgacacgctc ccgagttgtg cggtycgcygc cggcctctcg 900
 cggccagact acgcgctgct ggccaccgc cagctggtgc gcaccgactg ccccggcgac 960
 gcgctcttcg acctgctgcy cactggcgc cacttcaccg cgactgttaa gccaaacct 1020
 10 gccaggagtg totctaagag atccaggagg gagccacccc caaggacct gccagccaca 1080
 gacctccaa 1089

<210> 47

<211> 747

15 <212> DNA

<213> Homo sapiens

<400> 47

atgggtggcc cccggggcgc gggtgggtg gggcgggccc tctgtctcgg cgcggggcgc 60
 20 tgcactgca ttacaggt gacccgggt cggcgggcgg gcgaccgga gctcgggata 120
 cgtctctcga agtcgcga agacttaact gatggttcat atgatgatgt tctaatgct 180
 gaacaacttc aqaactcct ttacctgctg gagtcaacgg aggatcctgt aattattgaa 240
 agagctttga ttactttggg taacaatgca gccttttcag ttaaccaagc tattattcgt 300
 gaattgggtg gtattccaat tgttgcaaac aaaatcaacc attccaacca gattattaaa 360
 25 gagaagctt taatgcact aaataacctg agtgtgaatg ttgaaatca aatcaagata 420
 aagggtgcaag ttttgaact gcttttgaat ttgtctgaaa atccagccat gacagaagga 480
 cttctccgtg cccaagtga ttcatcattc ctttcccttt atgacagcca cgtagcaaa 540
 gagattcttc ttcgagta ctacctatct cagaatataa agaaactgct caaatagaa 600
 ggccatttag ctgtgcagcc tactttcact gaaggttcat tgttttccct gttacatgga 660
 30 gaagaatgcy cccagaaaat aagagcttta gttgatcacc atgatgcaga ggtgaaggaa 720
 aagggtgtaa caataatacc caaantc 747

<210> 48

<211> 294

35 <212> DNA

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<213> Homo sapiens

<400> 48

5 atggcgtegc tcctgtgctg tgggcogaag ctggcgcct gcggcatcgt cctcagcgcc 60
 tggggagtga tcattgtgat aatgetcgga atatttttca atgtccattc cgtgtgttg 120
 attgaggacg ttcccttcac ggagaaagat ttgagaatg gccccagaa catatacaac 180
 ctttacgagc aagtcagota caactgttcc atcgtgcag gcctttacct cctcctcgga 240
 ggcttctctt tctgccaagt tgggtcaat aagcgcaagg aatacatggt gcgc 294

10 <210> 49

<211> 516

<212> DNA

<213> Homo sapiens

15 <400> 49

atggcgggccc ccgcgcgcgc gcggcggtcg cggccgctgy cagcgtggc cctggctctg 60
 gcgcrggccc cggggctgcc cacagcccgg gccgggcaga caccgcgcgc tgcgagcgg 120
 gggccccag tgcggctttt cacagaggag gagctggccc gctatggcgg ggaggaggaa 180
 gatcagccca tctacttggc agtgaaggga gtggtgttg atgtaccctc cggaaaggag 240
 20 ttttatggac gaggagcccc ctacaatgcc ttgacgggga aggactccac tagaggggta 300
 gccaaagatgt ccttggatcc tgcagacctc acccatgaca ctacgggtct caccggcaag 360
 gaactggagg ccctggatga ggtcttcacc aaagtgtaca aagccaaata ccccatcgtc 420
 ggctacactg cccggagaat tctcaatgag gatggcagcc ctaacctgga cttcaagcct 480
 gaagaccagc cccattttga catcaaggat gagttc 516

25

<210> 50

<211> 360

<212> DNA

<213> Homo sapiens

30

<400> 50

atgatgccgt cccgtaccaa cctggctact ggaatcccca gtagtaaggt gaaatattca 60
 aggetctcca gcacagacga tggtacatt gacctcagt ttaagaaaac cctcctaag 120
 atcccttata aggcctcgc acctgccact gtgctgtttt tgattggcgc ctttctcatt 180
 35 attatacgtc cctcctgct gtcaggctac atcagcaag ggggggcaga ccgggcctg 240

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ccagtgtga tcattggcat tctggtgttc ctaccggat ttaccacct gcgcacgct 300
tactatgcat ccaaaggcta ccgtggttac tctatgatg acattccaga ctttgatgac 360

<210> 51
5 <211> 1065
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
10 <222> (2)...(943)

<400> 51
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Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly
15 1 5 10 15
tgg agt aca gat gag gct aat act tac ttc aag gaa tgg acc tgt tct 97
Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser
20 20 25 30
tcg tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gac gaa tgt 145
Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys
25 35 40 45
cct agt gca ttt gat ggc ctg tat ttt ctc cgc act gag aat ggt gtt 193
Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val
50 55 60
atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241
Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr
65 70 75 80
ctg gtg gcc agc gtg cat gag aat gac atg cgt ggg aag tgc acg gtg 289
Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val
30 85 90 95
ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 337
Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu
100 105 110
ggg gac ggc aac tgg gcc aac tac aac acc ttt gga tct gca gag gcg 385
35 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala

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	115	120	125	
	gcc acg agc gat gac tac aag aac cct gcc tac tac gac atc cag gcc	433		
	Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala			
	130	135	140	
5	aag gac ctg gcc atc tgg cac gtg ccc aat aag tcc ccc atg cag cac	481		
	Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His			
	145	150	155	160
	tgg aga aac agc tcc ctg ctg agg tac cgc acg gac act gcc ttc ctc	529		
	Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu			
10	165	170	175	
	cag aca ctg gga cat aat ctg ttt gcc atc tac cag aaa tat cca gtg	577		
	Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val			
	180	185	190	
	aaa tat gga gaa gga aag tgt tgg act gac aac gcc ccg gtg atc cct	625		
15	Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro			
	195	200	205	
	gtg gtc tat gat ttt gcc gac gcc cag aaa aca gca tct tat tac tca	673		
	Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser			
	210	215	220	
20	ccc tat gcc cag cgg gaa ttc act gcg gga ttt gtt cag ttc agg gta	721		
	Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val			
	225	230	235	240
	ttt aat aac gag aga gca gcc aac gcc ttg tgt gct gga atg agg gtc	769		
	Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val			
25	245	250	255	
	acc gga tgt aac act gag cac cac tgc att ggt gga gga gga tac ttt	817		
	Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe			
	260	265	270	
	cca gag gcc agt ccc cag cag tgt gga gat ttt tct ggt ttt gat tgg	865		
30	Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp			
	275	280	285	
	agt gga tat gga act cat gtt ggt tac agc agc agc cgt gag ata act	913		
	Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr			
	290	295	300	
35	gag gca gct gtg ctt cta ttc tat cgt tgagagtttt gtgggagggg	960		

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Glu Ala Ala Val Leu Leu Phe Tyr Arg
 305 310
 acccagacct ctctctccaa ccatgagatc ccaaggatgg agaacaactt acccagtagc 1020
 tagaatgtta atggcagaag agaaaacaat aaatcatatt gactc 1065

5
 <210> 52
 <211> 937
 <212> DNA
 <213> Homo sapiens

10
 <220>
 <221> CDS
 <222> (177)...(866)

<400> 52

15 cttttggaga actgcgttc tctttggag ggagtgttcg ccgcgcgcgc ggccgccacc 60
 tggagtttct teagactcca gatttcctg tcaaccacga ggagtccaga gaggaaacgc 120
 ggagcggaga caacagtacc tgacgctct ttcagcccg gatgcacca gcaggg 176
 atg ggc gac aag atc tgg ctg ccc ttc ccc gtg ctc ctt ctg gcc gct 224
 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala

20 1 5 10 15
 ctg cct ccg gtg ctg ctg cct ggg gcg gcc gcc ttc aca cct tcc ctc 272
 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu

25 20 25 30
 gat agc gac ttc acc ttt acc ctt ccc gcc gcc cag aag gag tgc ttc 320
 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe

35 40 45
 tac cag ccc atg ccc ctg aag gcc tcg ctg gag atc gag tac caa gtt 368
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val

50 55 60
 tta gat gga gca gga tta gat att gat ttc cat ctt gcc tct cca gaa 416
 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

65 70 75 80
 ggc aaa acc tta gtt ttt gaa caa aga aaa tca gat gga gtt cac act 464
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr

35 85 90 95

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	gta gag act gaa gtt ggc gat tac atg ttc tgc ttt gac aat aca ttc	512
	Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe	
	100 105 110	
	agc acc att tct gag aag gtg att ttc ttt gaa tta atc ctg gat aat	560
5	Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn	
	115 120 125	
	atg gga gaa cag gca caa gaa caa gaa gat tgg aag aaa tat att act	608
	Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr	
	130 135 140	
10	ggc aca gat ata ttg gat atg aaa ctg gaa cac atc ctg gaa tcc atc	656
	Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile	
	145 150 155 160	
	aac agc atc aag tcc aga cta agc aaa agt ggg cac ata caa att ctg	704
	Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu	
15	165 170 175	
	ctt aga gca ttt gaa gct cgt gat cga aac ata caa gaa agc aac ttt	752
	Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe	
	180 185 190	
	gat aga gtc aat ttc tgg tct atg gtt aat tta gtg gto atg gtg gtg	800
20	Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val	
	195 200 205	
	gtg tca gcc att caa gtt tat atg ctg aag agt ctg ttt gaa gat aag	848
	Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys	
	210 215 220	
25	agg aaa agt aga act taaaactcca aactagagta cgtaacattg aaaaatg	900
	Arg Lys Ser Arg Thr	
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	aggcataaaa atgcaataaa ctgttacagt caagacc	937
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	Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu	
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	ctg ttg ctg ctg ctg ccg ccg ccg ccg tgc cct gcc cac agc gcc acg	151
	Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr	
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	Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala	
	35 40 45	
	tgg ttt gac cag gcc aag ttc ggc atc ttc atc cac tgg gga gtg ttt	247
15	Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe	
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	tcc gtg ccc agc ttc ggt agc gag tgg ttc tgg tgg tat tgg caa aag	295
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys	
	65 70 75 80	
20	gaa aag ata ccg aag tat gtg gaa ttt atg aaa gat aat tac cct cct	343
	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro	
	85 90 95	
	agt ttc aaa tat gaa gat ttt gga cca cta ttt aca gca aaa ttt ttt	391
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	
25	100 105 110	
	aat gcc aac cag tgg gca gat att ttt cag gcc tct ggt gcc aaa tac	439
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	
	115 120 125	
	att gtc tta act tcc aaa cat cat gaa ggc ttt acc ttg tgg ggg tca	487
30	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser	
	130 135 140	
	gaa tat tgg tgg aac tgg aat gcc ata gat gag ggg ccc aag agg gac	535
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp	
	145 150 155 160	
35	att gtc aag gaa ctt gag gta gcc att agg aac aga act gac ctg cgt	583

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	ttt gga ctg tac tat tcc ctt ttt gaa tgg ttt cat ccg ctc ttc ctt	631
	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu	
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	gag gat gaa tcc agt tca ttc cat aag cgg caa ttt cca gtt tct aag	679
	Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys	
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	aca ttg cca gag ctc tat gag tta gtg aac aac tat cag cct gag gtt	727
10	Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val	
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	ctg tgg tcc gat ggt gac gga gga gca ccg gat caa tac tgg aac agc	775
	Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser	
	225 230 235 240	
15	aca ggc ttc ttg gcc tgg tta tat aat gaa agc cca gtt cgg ggc aca	823
	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr	
	245 250 255	
	gta gtc acc aat gat cgt tgg gga gct ggt agc atc tgt aag cat ggt	871
	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly	
20	260 265 270	
	ggc ttc tat acc tgc agt gat cgt tat aac cca gga cat ctt ttg cca	919
	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro	
	275 280 285	
	cat aaa tgg gaa aac tgc atg aca ata gac aaa ctg tcc tgg ggc tat	967
25	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr	
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	agg agg gaa gct gga atc tct gac tat ctt aca att gaa gaa ttg gtg	1015
	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val	
	305 310 315 320	
30	aag caa ctt gta gag aca gtt tca tgt gga gga aat ctt ttg atg aat	1063
	Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn	
	325 330 335	
	att ggg ccc aca cta gat ggc acc att tct gta gtt ttt gag gag cga	1111
	Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg	
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5  Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val
      370              375              380
tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ctt      1255
Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu
      385              390              395              400
10  aaa tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att      1303
Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile
      405              410              415
ctg ggg gca aca gag gtg aaa cta ctg ggc cat gga cag cca ctt aac      1351
Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn
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tgg att tot ttg gag caa aat ggc att atg gta gaa ctg cca cag cta      1399
Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu
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acc att cat cag atg ccg tgt aaa tgg ggc tgg gct cta gcc ctg act      1447
20  Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr
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Asn Val Ile
465
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agaaaattat tttggcagtt cagcccttcc cctttttccc actaaatttt ttcttaaatt      1620
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Met	
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gat aac gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg	164
Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val	
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10 aaa ggc cac gtg aag atg ctg cgg ctg gat att atc aac tca ctg gta	212
Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu Val	
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aca aca gta ttc atg ctc atc gta tct gtg ttg gca ctg ata cca gaa	260
Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Glu	
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acc aca aca ttg aca gtt ggt gga ggg gtg ttt gca ctt gtg aca gca	308
Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr Ala	
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gta tgc tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc	356
20 Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe	
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aat ccc agc ggt cct tac cag caa aag cct gtg cat gaa aaa aaa gaa	404
Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys Glu	
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	gggtgctgcg gattgaggtc ccggttcta acgaatctct gctggatttg ccgtaacct	180
	gtcccgagc gggtcacag ggtctgaagg ccacgatga ggcaaggta aagttctgag	240
	ccaccgggtg cctccttccc aggaactgcaa g atg gag gaa ggc ggg aac cta	292
	Met Glu Glu Gly Gly Asn Leu	
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	gga ggc ctg att aag atg gtc cat cta ctg gtc ttg tca ggt gcc tgg	340
	Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp	
	10 15 20	
	ggc atg caa atg tgg gtg acc ttc gtc tca ggc ttc ctg ctt ttc cga	388
15	Gly Met Gln Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg	
	25 30 35	
	agc ctt ccc cga cat acc ttc gga cta gtg cag agc aaa ctc ttc ccc	436
	Ser Leu Pro Arg His Thr Phe Gly Leu Val Gln Ser Lys Leu Phe Pro	
	40 45 50 55	
20	ttc tac ttc cac atc tcc atg ggc tgt gcc ttc atc aac ctc tgc atc	484
	Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile	
	60 65 70	
	ttg gct tca cag cat gct tgg gct cag ctc aca ttc tgg gag gcc agc	532
	Leu Ala Ser Gln His Ala Trp Ala Gln Leu Thr Phe Trp Glu Ala Ser	
25	75 80 85	
	cag ctt tac ctg ctg ttc ctg agc ctt acg ctg gcc act gtc aac gcc	580
	Gln Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala	
	90 95 100	
	cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc	628
30	Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Gln Thr	
	105 110 115	
	gtg gag aag gag cga ggc ctg ggt ggg gag gta cca ggc agc cac cag	676
	Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Gln	
	120 125 130 135	
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	75 80 85	
	cag tac tat ggg gct ggg gtg gcc aga gac cca ggg ttc cgc ago aac	461
	Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn	
	90 95 100	
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	Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala	
	105 110 115 120	
	cag cag gtg tgg gga acc ctt gtc ctt cta cag agg ctg gag cca gta	557
	Gln Gln Val Trp Gly Thr Leu Val Leu Leu Gln Arg Leu Glu Pro Val	
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	His Leu Gln Leu Gln Cys Met Ser Gln Glu Gln Leu Ala Gln Val Ala	
	140 145 150	
	gcc aat gct acc aag gaa ttc act gag gcc ttc ctg gga tgc cgc gcc	653
20	Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala	
	155 160 165	
	atc cac ccc cgc tgc cgc tgg gga gcg gcg cct tat cgg ggc cgc ccg	701
	Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro	
	170 175 180	
25	aag ctg ctg cag ctg ccg ctg gga ttc ttg tac gtg cat cac acc tac	749
	Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr	
	185 190 195 200	
	gtg cct gca cca ccc tgc acg gac ttc acg cgc tgc gca gcc aac atg	797
	Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met	
30	205 210 215	
	cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc	845
	Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile	
	220 225 230	
	ggc tac agt ttc gtg gtg ggc tcg gac ggc tac gtg tac gag gga cgc	893
35	Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg	

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	235	240	245	
	ggc tgg cac tgg gtg ggc gcc cac acg ctc ggc cac aac tcc cgg ggc			941
	Gly Trp His Trp Val Gly Ala His Thr Leu Gly His Asn Ser Arg Gly			
	250	255	260	
5	ttc ggc gtg gcc ata gtg ggc aac tac acc gcg gcg ctg ccc acc gag			989
	Phe Gly Val Ala Ile Val Gly Asn Tyr Thr Ala Ala Leu Pro Thr Glu			
	265	270	275	280
	gcc gct ctg cgc acg gtg cgc gac acg ctc ccg agt tgt gcg gtg cgc			1037
	Ala Ala Leu Arg Thr Val Arg Asp Thr Leu Pro Ser Cys Ala Val Arg			
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	gcc ggc ctc ctg cgg cca gac tac gcg ctg ctg ggc cac cgc cag ctg			1085
	Ala Gly Leu Leu Arg Pro Asp Tyr Ala Leu Leu Gly His Arg Gln Leu			
	300	305	310	
	gtg cgc acc gac tgc ccc ggc gac gcg ctc ttc gac ctg ctg cgc acc			1133
15	Val Arg Thr Asp Cys Pro Gly Asp Ala Leu Phe Asp Leu Leu Arg Thr			
	315	320	325	
	tgg ccg cac ttc acc gcg act gtt aag cca aga cct gcc agg agt gtc			1181
	Trp Pro His Phe Thr Ala Thr Val Lys Pro Arg Pro Ala Arg Ser Val			
	330	335	340	
20	tct aag aga tcc agg agg gag cca ccc cca agg acc ctg cca gcc aca			1229
	Ser Lys Arg Ser Arg Arg Glu Pro Pro Pro Arg Thr Leu Pro Ala Thr			
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	gcccgccggg cagc atg ggt ggc ccc cgg ggc gcg ggc tgg gtg gcg gcg	170
	Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala	
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5	ggc ctg ctg ctc ggc gcg ggc gcc tgc tac tgc att tac agg ctg acc	218
	Gly Leu Leu Leu Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr	
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	cgg ggt cgg cgg cgg ggc gac cgc gag ctc ggg ata cgc tct teg aag	266
	Arg Gly Arg Arg Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys	
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	tcc gca gaa gac tta act gat ggt tca tat gat gat gtt cta aat gct	314
	Ser Ala Glu Asp Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala	
	45 50 55 60	
	gaa caa ctt cag aaa ctc ctt tac ctg ctg gag tca acg gag gat cct	362
15	Glu Gln Leu Gln Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro	
	65 70 75	
	gta att att gaa aga gct ttg att act ttg ggt aac aat gca gcc ttt	410
	Val Ile Ile Glu Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe	
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	Ser Val Asn Gln Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val	
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	gca aac aaa etc aac cat tcc aac cag agt att aaa gag aaa gct tta	506
	Ala Asn Lys Ile Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu	
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	aat gca cta aat aac ctg agt gtg aat gtt gaa aat caa atc aag ata	554
	Asn Ala Leu Asn Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile	
	125 130 135 140	
	aag gtg caa gtt ttg aaa ctg ctt ttg aat ttg tct gaa aat cca gcc	602
30	Lys Val Gln Val Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala	
	145 150 155	
	atg aca gaa gga ctt ctc cgt gcc caa gtg gat tca tca ttc ctt tcc	650
	Met Thr Glu Gly Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser	
	160 165 170	
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 Leu Phe Gln Asn Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala
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 gtg cag cct act ttc act gaa ggt tca ttg ttt ttc ctg tta cat gga 794
 Val Gln Pro Thr Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly
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 gaa gaa tgt gcc cag aaa ata aga gct tta gtt gat cac cat gat gca 842
 10 Glu Glu Cys Ala Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala
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 Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile Val Leu Ser
 30 5 10 15
 gcc tgg gga gtg atc atg ttg ata atg ctc gga ata ttt ttc aat gtc 152
 Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Phe Asn Val
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	Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln Val Ser Tyr			
	55 60 65			
5	aac tgt ttc atc gct gca ggc ctt tac ctc ctc ctc gga ggc ttc tct	296		
	Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser			
	70 75 80			
	ttc tgc caa gtt cgg ctc aat aag cgc aag gaa tac atg gtg cgc	341		
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	tagggcccc ggagcgtttc cccgctccag cccctctctct atttaaagac tccctgcacc	400		
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	cgtgtt atg atg ccg tcc cgt acc aac ctg gct act gga atc ccc agt	168
	Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser	
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	agt aaa gtg aaa tat tca agg ctc tcc agc aca gac gat ggc tac att	216
10	Ser Lys Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile	
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	gac ctt cag ttt aag aaa acc cct cct aag atc cct tat aag gcc atc	264
	Asp Leu Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile	
	35 40 45	
15	gca ctt gcc act gtg ctg ttt ttg att ggc gcc ttt ctc att att ata	312
	Ala Leu Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile	
	50 55 60	
	ggc tcc ctc ctg ctg tca ggc tac atc agc aaa ggg ggg gca gac cgg	360
	Gly Ser Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg	
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	gcc gtt cca gtg ctg atc att ggc att ctg gtg ttc cta ccc gga ttt	408
	Ala Val Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe	
	80 85 90	
	tac cac ctg cgc atc gct tac tat gca tcc aaa ggc tac cgt ggt tac	456
25	Tyr His Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr	
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	tcc tat gat gac att cca gac ttt gat gac tagcaccac ccca	500
	Ser Tyr Asp Asp Ile Pro Asp Phe Asp Asp	
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	gctgaggact aaggaattct gcagcttgca gatgtttaag aaaataatgg ccagattttt	620
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35	taaatagtct tcattgcca tttgttcttg tagcaaatgg aacaatgtgg tatggcta	860

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ttcttattat taagtagttt attttaaaaa tatctgagta tattatcctg tacacttate 920
 cctacettca tgttccagtg gaagacctta gtaaaatcaa agatcagtga gttcatctgt 980
 aatatttttt ttacttgctt tcttactgac agcaaccagg aattttttta tctgcagag 1040
 caagttttca aaatgtaaat acttccctctg tttaacagtc cttggaccat tctgatccag 1100
 5 ttcaccagta ggttggacag catataattt gcatcatttt gtcccttgta aatcaagatg 1160
 ttctgcagat tattccttta acggccggac ttttggctgt ttccaatga aacatgtagt 1220
 ggttattatt tagagtttat agccgtattg ctagcacett gtagtatgto atcattctgc 1280
 tcatgattcc aaggatcagc ctggatgect agaggactag atcaccttag tttgatteta 1340
 ttttttagct tgcaaaaagt gacttatatt ccaaagaaat taaaatggtg aaatccaat 1400
 10 cctagaaata aaatgagtta acttc 1425

<210> 61

<211> 307

<212> PRT

15 <213> Homo sapiens

<400> 61

Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp Gly Leu
 1 5 10 15
 20 Pro Leu Ser Ala Ser Thr Asp Tyr Glu Gln Ser Thr Gly Met Gln Glu
 20 25 30
 Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln Leu Pro
 35 40 45
 Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser
 25 50 55 60
 Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr Pro Asn
 65 70 75 80
 Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe Ile Thr
 85 90 95
 30 Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe
 100 105 110
 Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr Asn Asn
 115 120 125
 Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln Thr Glu
 35 130 135 140

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Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser
 145 150 155 160
 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly
 165 170 175
 5 Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly
 180 185 190
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile
 195 200 205
 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp
 10 210 215 220
 Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys Leu Tyr
 225 230 235 240
 Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val Lys Ser
 245 250 255
 15 Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu
 260 265 270
 Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly Ala Phe
 275 280 285
 Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala Pro Asp
 20 290 295 300
 Tyr Asp Val
 305
 <210> 62
 25 <211> 183
 <212> PRT
 <213> Homo sapiens
 <400> 62
 30 Met Thr Ala Gln Gly Gly Leu Val Ala Asn Arg Gly Arg Arg Phe Lys
 1 5 10 15
 Trp Ala Ile Glu Leu Ser Gly Pro Gly Gly Gly Ser Arg Gly Arg Ser
 20 25 30
 Asp Arg Gly Ser Gly Gln Gly Asp Ser Leu Tyr Pro Val Gly Tyr Leu
 35 35 40 45

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Asp Lys Gln Val Pro Asp Thr Ser Val Gln Glu Thr Asp Arg Ile Leu
  50              55              60
Val Glu Lys Arg Cys Trp Asp Ile Ala Leu Gly Pro Leu Lys Gln Ile
  65              70              75              80
5  Pro Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile
      85              90              95
Phe Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala
      100              105              110
Leu Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln
10      115              120              125
Lys Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu
      130              135              140
Ala Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His
      145              150              155              160
15  Ala Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Phe
      165              170              175
Ser Gly Gly Gly Leu Leu Leu
      180

20  <210> 63
    <211> 327
    <212> PRT
    <213> Homo sapiens

25  <400> 63
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  1              5              10              15
Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Ala Arg Pro Ser Ser Ala
      20              25              30
30  Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro Pro Leu Arg Glu
      35              40              45
Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His Asn Ile Ser Leu
      50              55              60
Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile Thr Leu Glu Arg
35  65              70              75              80

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Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr Ser Gly Asp Leu
 85 90 95
 Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu Gln Leu Glu Asn
 100 105 110
 5 Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr Thr Gln Tyr Arg
 115 120 125
 Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe
 130 135 140
 Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Glu
 10 145 150 155 160
 Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr
 165 170 175
 Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp
 180 185 190
 15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn
 195 200 205
 Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr Lys Leu Lys Ile
 210 215 220
 Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp Cys Arg Ala Leu
 20 225 230 235 240
 Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu Val Val Leu Ser
 245 250 255
 Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val Ala Glu Val Ile
 260 265 270
 25 Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr Thr Gln Lys Lys
 275 280 285
 Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln Ile Glu Gln Leu
 290 295 300
 Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val Pro Arg His Arg
 30 305 310 315 320
 Lys Asn, Glu Ser Leu Gly Gln
 325

<210> 64

35 <211> 223

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<212> PRT

<213> Homo sapiens

<400> 64

5 Met Lys Phe Val Pro Cys Leu Leu Leu Val Thr Leu Ser Cys Leu Gly
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 Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Glu Glu
 20 25 30
 Phe His Phe Gln Thr Gly Gly Arg Asp Ser Cys Thr Met Arg Pro Ser
 10 35 40 45
 Ser Leu Gly Gln Gly Ala Gly Glu Val Trp Leu Arg Val Asp Cys Arg
 50 55 60
 Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser Met
 65 70 75 80
 15 Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala Leu
 85 90 95
 Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val Leu
 100 105 110
 Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln Gln
 20 115 120 125
 Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro Glu
 130 135 140
 Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr Glu
 145 150 155 160
 25 Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala Lys
 165 170 175
 Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg Pro
 180 185 190
 Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp Lys
 30 195 200 205
 Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly
 210 215 220

<210> 65

35 <211> 48

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<212> PRT

<213> Homo sapiens

<400> 65

5 Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg
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 Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys
 20 25 30
 Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser
 10 35 40 45

<210> 66

<211> 371

<212> PRT

15 <213> Homo sapiens

<400> 66

Met Ala Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val
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 20 Thr Gly Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met
 20 25 30
 Ala Glu Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe
 35 40 45
 Leu Gln Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala
 25 50 55 60
 Phe Tyr Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val
 65 70 75 80
 Asp Pro Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu
 85 90 95
 30 Cys Asp Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr
 100 105 110
 Ser Ala Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr
 115 120 125
 Gly Leu Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln
 35 130 135 140

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Trp Leu Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu
 145 150 155 160
 Ala Asp Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val
 165 170 175
 5 Ile Thr Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile
 180 185 190
 Gln Met Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro
 195 200 205
 Leu Arg Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser
 10 210 215 220
 Leu Leu Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly
 225 230 235 240
 Asn Pro Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val
 245 250 255
 15 Gly Gln Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser
 260 265 270
 Ile Ala Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser
 275 280 285
 Ala Thr Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp
 20 290 295 300
 Ala Leu Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile
 305 310 315 320
 Leu Gly Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu
 325 330 335
 25 His Arg Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu
 340 345 350
 Glu Ser Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn
 355 360 365
 Asp Ala Ser
 30 370

<210> 67

<211> 90

<212> PRT

35 <213> Homo sapiens

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<400> 67
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 5 Leu Asn Ser Ile Tyr Gln Cys Pro Glu His Ser Gln Leu Thr Thr Leu
 20 25 30
 Gly Val Asp Gly Lys Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr
 35 40 45
 Phe Ile Ala Gly Ala Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp
 10 50 55 60
 Pro Val Asp Asn Ile Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met
 65 70 75 80
 Gln Leu His Leu Arg Ala Thr Ile Arg Met
 85 90
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 <210> 68
 <211> 499
 <212> PRT
 <213> Homo sapiens
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 Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys
 25 20 25 30
 Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu
 35 40 45
 Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val
 50 55 60
 30 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe
 65 70 75 80
 Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile
 85 90 95
 Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg
 35 100 105 110

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Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr
 115 120 125
 Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu
 130 135 140
 5 Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile
 145 150 155 160
 Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val
 165 170 175
 Ile Pro Pro Phe Val Phe Met Val Thr Glu Gly Trp Asn Tyr Ile Glu
 10 180 185 190
 Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp
 195 200 205
 Phe Val Ala Gly Val Asn Pro Ser Ala Asn Tyr His Ala Leu Tyr Arg
 210 215 220
 15 Tyr Phe Val Glu Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu
 225 230 235 240
 Phe Val Asn Trp Lys Val Ser Met Phe Val Glu Val His Lys Ala Ile
 245 250 255
 Lys Lys Arg Arg Arg Arg Arg Lys Glu Ser Phe Glu Ser Ser Pro His
 20 260 265 270
 Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val
 275 280 285
 Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu
 290 295 300
 25 Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu
 305 310 315 320
 Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala
 325 330 335
 Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val
 30 340 345 350
 Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val
 355 360 365
 Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser
 370 375 380
 35 Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu

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385 390 395 400
 Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln
 405 410 415
 Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu
 5 420 425 430
 Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser
 435 440 445
 Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe
 450 455 460
 10 Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser
 465 470 475 480
 Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro
 485 490 495
 Lys Gly Thr
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 <210> 69
 <211> 106
 <212> PRT
 20 <213> Homo sapiens

 <400> 69
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 25 Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr Arg Glu Lys Leu Thr Pro
 20 25 30
 Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Ala Gln Trp Gln Lys
 35 40 45
 Val Leu Pro Arg Arg Arg Thr Arg Asn Ile Val Thr Gly Leu Gly Ile
 30 50 55 60
 Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr Thr Phe Tyr Ser Ile Ser
 65 70 75 80
 Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp Glu Ala Lys Ala Ala Arg
 85 90 95
 35 Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser

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100

105

5 <210> 70
 <211> 152
 <212> PRT
 <213> Homo sapiens

 <400> 70
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 Glu Thr His Phe Thr Val Ile Ile Thr Ser Val Gly Leu Glu Lys Leu
 20 25 30
 Ala Gln Lys Gly Lys Ser Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile
 35 40 45
 15 Ser Leu Phe Leu Ile Ile Ser Met Cys Leu Leu Phe Leu Trp Lys Lys
 50 55 60
 Tyr Gln Pro Tyr Lys Val Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu
 65 70 75 80
 Thr Glu Tyr Arg Lys Ala Gln Thr Phe Ser Gly His Glu Asp Ala Leu
 20 85 90 95
 Asp Asp Phe Gly Ile Tyr Glu Phe Val Ala Phe Pro Asp Val Ser Gly
 100 105 110
 Val Ser Arg Ile Pro Ser Arg Ser Val Pro Ala Ser Asp Cys Val Ser
 115 120 125
 25 Gly Gln Asp Leu His Ser Thr Val Tyr Glu Val Ile Gln His Ile Pro
 130 135 140
 Ala Gln Gln Gln Asp His Pro Glu
 145 150

 30 <210> 71
 <211> 921
 <212> DNA
 <213> Homo sapiens

 35 <400> 71

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 tcgaggaaac ttgctcaact tcctgataga tgtacactga aaactggaca ttataacatt 180
 aattttatta gctctctggg agtgagctac atgatgttgt gcactgaaaa ttaccacaat 240
 5 gttctcgcct tctctttcct ggatgagctt cagaaggagt tcattactac ttataacatg 300
 atgaagacaa atactgtgt cagaccatac tgtttcattg aatttgataa cttcattcag 360
 aggaccaagc agcgatataa taatcccagg tctctttcaa caaagataaa tctttctgac 420
 atgcagacgg aaatcaagct gaggcctcct tatcaaatth ccattgtgcga actgggggtca 480
 gccaatggag tcacatcagc atttctgtt gactgtaaag gtgctggtaa gatttcttct 540
 10 gctcaccagc gactggaaac agcaactctg tcagggtattg taggatttat ccttagtctt 600
 ttatgtggag ctctgaattt aattcgaggg tttcatgcta tagaaagtct cctgcagagt 660
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 ggcttaactc gtctatgcaa catgtatctc tatgaactgc gaacactctg gaagcttttc 840
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<210> 72

<211> 549

20 <212> DNA

<213> Homo sapiens

<400> 72

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 tcgctctacc cagtcgggta cttggacaag caagtgcctg ataccagcgt gcaagagaca 180
 gaccggatcc tgggtggagaa gcgctgctgg gacatcgctt tgggtccctt caaacagatt 240
 cccatgaata tcttcatcat gtacatggca ggcaatacta tctccatctt ccttactatg 300
 atggtgtgta tgatggcctg gcgacccatt caggcaccta tggccatttc agccaatttc 360
 30 aagatgttag aaagttcaag ccagaagttt cttcagggtt tggctctatct cattgggaac 420
 ctgatgggtt tggcattggc tgtttacaag tgccagtcca tgggactgtt acctacacat 480
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 ctgcttttg 549

35 <210> 73

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<211> 981
<212> DNA
<213> Homo sapiens

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15 aatgtcaaa attgttttcc tttaaatgg accgtgtaca gtatgaatgg gagtgtaaag 600
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aaaaatgagt ctctgggcca g 981

<210> 74
25 <211> 669
<212> DNA
<213> Homo sapiens

<400> 74
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gattcctgca ctatgcgtcc cagcagcttg gggcaagggt ctggagaggt ctggcttcgc 180
gtcgactgcc gcaacacaga ccagacctac tgggtgaggt acagggggca gccagcatg 240
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35 cgccltcacc atgcgtgcca gggggcccg gtgcttaggc catccgtgtg caggaggct 360

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	gcaacacagc	tgggaaagga	ctcgatggaa	gagctgggaa	aagccaaacc	caccaccoga	540
	cccacagcca	aacctaccca	gcctggaccc	aggcccgag	ggaatgagga	agcaagaag	600
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	<213> Homo sapiens						
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	gagcacagct	tccagcatcc	cttcctccag	gcagtgggca	tgctctggg	agaattctcc	180
	tgcctggctg	ccttctacct	cctccgatgc	agagctgcag	ggcaatcaga	ctccagcgt	240
	gaccccaagc	agcccttcaa	ccctcttctt	ttcctgcccc	cagcgtctctg	tgacatgaca	300
	gggaccagcc	tcattgtatg	ggctctgaac	atgaccagtg	ccccagctt	ccagatgctg	360
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	ctgttgatca	tcattggcca	gatcatcggt	gccatccaga	tggcgctaga	ggagaagttc	600
	gtctacaaac	acaatgtgca	cccaactggg	gcagttggca	ctgagggcct	ctttgcttt	660
35	gtgatctct	ccctgctgct	ggtgcccatg	tactacatcc	ccgcggctc	cttcagcgga	720

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	aacctctgtg ggacactgga ggatgcattg gacgccttct gccaggtggg coagcagccg	780
	ctcattgcog tggcaactgt gggcaacatc agoagcattg ccttcttcaa cttcgcaggo	840
	atcagcgtca ccaaggaaact gagcgccacc acccgcatgg tgttggacag cttgcgcacc	900
	gttgcacatc gggcactgag cctggcactg ggtgggagg ccttccatgc actgcagatc	960
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	<213> Homo sapiens	
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	taccagtgcc ctgagcacag tcaactgaca actctgggag tggatgggaa ggagtcccca	120
	gaggtccact tgggccagtg gtactttatc gcaggggcag ctcccaccaa ggaggagtgtg	180
	gcaacttttg accctgtgga caacattgtc ttcaatatgg ctgtggctc tgccccgatg	240
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	<213> Homo sapiens	
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	cagaagctgc atctgctcaa ggagtcccg tgccctgggtc aggagggcct ggacaagatc	180
30	ctagagggtg tatctgatgc tgcaggacag ggtgtggcca tcacagggaa ccagaccttc	240
	aacaactgga actggcccaa tgcantgatt ttgcagcga ccgtcattac caccattgga	300
	tatggcaatg tggctcccaa gaccccgcc ggtcgctctc tctgtgtttt ctatggtctc	360
	ttcgggggtg cgctctgcct gacgtggatc agtgcctcg gcaagttctt cgggggacgt	420
	gccnagagac tagggcagtt ccttaccag agaggtgtga gtctgcggaa ggcgcagatc	480
35	acgtgcacag tcacttccat cgtgtggggc gtccatagtc acctggtgat cccacccttc	540

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 15 atgggcgagt tccctctc ctccgagtc accctcacca gcactgagtc tgagctctct 1440
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<211> 318

20 <212> DNA

<213> Homo sapiens

<400> 79

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 gcgagcttg cccagtgga gaaggtcta ccacggcggc gaaccggga catcgtgacc 180
 ggcctaggca tcggggccct ggtgttggt atttatggtt acaccttcta ctcgatttcc 240
 caggagcgtt tcctagatga gctagaagac gaggccaaag ctgcccagc ccgagctctg 300
 gcaaggggcgt cagggtcc 318

30

<210> 80

<211> 456

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<213> Homo sapiens

35

80/177

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 cctttagcaa gtataactgg aatatcacta tttttgatta tatccatgtg tcttctcttc 180
 5 ctatggaaa aatatcaacc ctacaaagt ataaaacaga aactagaagg caggccagaa 240
 acagaataca ggaaagctca aacattttca ggccatgaag atgctctgga tgacttcgga 300
 atatatgaat ttgttgcttt tccagatgtt tctggtgttt ccaggatccc aagcaggtct 360
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 Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp
 1 5 10
 gga ctg cca ctt tct gct tct act gat tat gaa caa agc aca gga atg 155
 25 Gly Leu Pro Leu Ser Ala Ser Thr Asp Tyr Glu Gln Ser Thr Gly Met
 15 20 25 30
 cag gag tgc aga aag tat ttt aaa atg ctt tcg agg aaa ctt gct caa 203
 Gln Glu Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln
 35 40 45
 30 ctt cct gat aga tgt aca ctg aaa act gga cat tat aac att aat ttt 251
 Leu Pro Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe
 50 55 60
 att agc tct ctg gga gtg agc tac atg atg ttg tgc act gaa aat tac 299
 Ile Ser Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr
 35 65 70 75

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	cca aat gtt ctc gcc ttc tct ttc ctg gat gag ctt cag aag gag ttc	347
	Pro Asn Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe	
	80 85 90	
	att act act tat aac atg atg aag aca aat act gct gtc aga cca tac	395
5	Ile Thr Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr	
	95 100 105 110	
	tgt ttc att gaa ttt gat aac ttc att cag agg acc aag cag cga tat	443
	Cys Phe Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr	
	115 120 125	
10	aat aat ccc agg tct ctt tca aca aag ata aat ctt tct gac atg cag	491
	Asn Asn Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln	
	130 135 140	
	acg gaa atc aag ctg agg cct cct tat caa att tcc atg tgc gaa ctg	539
	Thr Glu Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu	
15	145 150 155	
	ggg tca gcc aat gga gtc aca tca gca ttt tct gtt gac tgt aaa ggt	587
	Gly Ser Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly	
	160 165 170	
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20	Ala Gly Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu	
	175 180 185 190	
	tca ggg att gta gga ttt atc ctt agt ctt tta tgt gga gct ctg aat	683
	Ser Gly Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn	
	195 200 205	
25	tta att cga ggc ttt cat gct ata gaa agt ctc ctg cag agt gat ggt	731
	Leu Ile Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly	
	210 215 220	
	gat gat ttt aat tac atc att gca ttt ttc ctt gga aca gca gcc tgc	779
	Asp Asp Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys	
30	225 230 235	
	ctt lac cag tgt tat tta ctt gtc tac tac acc ggc tgg cgg aat gtc	827
	Leu Tyr Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val	
	240 245 250	
	aaa tct ttt ttg act ttt ggc tta atc tgt cta tgc aac atg tat ctc	875
35	Lys Ser Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu	

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	255	260	265	270	
	tat gaa ctg cgc aac ctc tgg cag ctt ttc ttt cat gtg act gtg gga				923
	Tyr Glu Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly				
		275	280	285	
5	gca ttt gtt aca cta cag atc tgg cta agg caa gcc cag ggc aag gct				971
	Ala Phe Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala				
		290	295	300	
	ccc gat tat gat gtc tgacaccatc cttcagatct attgccttgg ctte				1020
	Pro Asp Tyr Asp Val				
10	305				
	agggggataa ggaggggaaca tatcataact gcactgtgat gaagaagctg tteccacag				1080
	aggaggaagct ctgctttctt tctctccaac ttctctttt taaaatcagc atgatgtgcc				1140
	tgtgagcatg gaagagtcct ctcagaagaa tgttggccat gagactatca ttcagaggag				1200
	gaggggattt ctctcttcaa ggcataaaca gtggaagasc agtcatatgc cattggaagt				1260
15	cttggccagc agtcctgaat ccttcctgaa gagttcagaa aatagatgtg gtattgctct				1320
	gaggaccagg caggaggaac tctacaacct gagtttgct ttgtgaggca ttagtataga				1380
	ccaaataaaa agctgcagaa attggaagt ttatgttta aataaatgac tgtgat				1436
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	cgaggctata ggacgcagct gttgcc atg acg gcc cag ggg ggc ctg gtg				110
30	Met Thr Ala Gln Gly Gly Leu Val				
	1 5				
	gct aac cga ggc cgg cgc ttc aag tgg gcc att gag cta agc ggg cct				158
	Ala Asn Arg Gly Arg Arg Phe Lys Trp Ala Ile Glu Leu Ser Gly Pro				
	10 15 20				
35	gga gga ggc agc agg ggt cga agt gac cgg ggc agt ggc cag gga gac				206

	Gly Gly Gly Ser Arg Gly Arg Ser Asp Arg Gly Ser Gly Gln Gly Asp	
	25 30 35 40	
	tgc ctc tac cca gtc ggt tac ttg gac aag caa gtg cct gat acc agc	254
	Ser Leu Tyr Pro Val Gly Tyr Leu Asp Lys Gln Val Pro Asp Thr Ser	
5	45 50 55	
	gtg caa gag aca gac cgg atc ctg gtg gag aag cgc tgc tgg gac atc	302
	Val Gln Glu Thr Asp Arg Ile Leu Val Glu Lys Arg Cys Trp Asp Ile	
	60 65 70	
	gcc ttg ggt ccc ctc aaa cag att ccc atg aat ctc ttc atc atg tac	350
10	Ala Leu Gly Pro Leu Lys Gln Ile Pro Met Asn Leu Phe Ile Met Tyr	
	75 80 85	
	atg gca ggc aac act atc tcc atc ttc cct act atg atg gtg tgt atg	398
	Met Ala Gly Asn Thr Ile Ser Ile Phe Pro Thr Met Met Val Cys Met	
	90 95 100	
15	atg gcc tgg cga ccc att cag gca ctt atg gcc att tca gcc act ttc	446
	Met Ala Trp Arg Pro Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe	
	105 110 115 120	
	aag atg tta gaa agt tca agc cag aag ttt ctt cag ggt ttg gtc tat	494
	Lys Met Leu Glu Ser Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr	
20	125 130 135	
	ctc att ggg aac ctg atg ggt ttg gca ttg gct gtt tac aag tgc cag	542
	Leu Ile Gly Asn Leu Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln	
	140 145 150	
	tcc atg gga ctg tta cct aca cat gca tgc gat tgg tta gcc ttc att	590
25	Ser Met Gly Leu Leu Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile	
	155 160 165	
	gag ccc cct gag aga atg gag ttc agt ggt gga gga ctg ctt ttg tgaac	640
	Glu Pro Pro Glu Arg Met Glu Phe Ser Gly Gly Gly Leu Leu Leu	
	170 175 180	
30	atgagaaagc agcgctgggt cctatgtat ttgggtcttta ttacatcct tctttaagcc	700
	cagtggctcc tcagcataact cttaaactaa tcacttatgt taanaagaaac caanaagactc	760
	ttttctccat ggtgggggtga caggctctag aaggacaatg tgcatattac gacaacacaca	820
	aagaaactat accataacccc aaggctgtaaa ataatgtaga aaactttatt tttgtttcca	880
	gtacagagca aaacaacaac aaaaaaacat aactatgtaa acaagagaat aactgtgtgt	940
35	aaatacaagaa ctgttcgcagc atctccttcc aataaattaa atggttgaga acaatgc	997

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5  <213> Homo sapiens
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acctcttgcc gcc atg cgc gcc ctc ccc gcc ctg ctg gag gcc agg gcg 169
Met Arg Ala Leu Pro Gly Leu Leu Glu Ala Arg Ala
15 1 5 10
cgt acg ccc cgg ctg ctc ctc ctc cag tgc ctt ctc gct gcc gcg cgc 217
Arg Thr Pro Arg Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Ala Arg
15 20 25
cca agc tcg gcg gac gcc agt gcc cca gat tcg cct ttt aca agt cca 265
20 Pro Ser Ser Ala Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro
30 35 40
cct ctc aga gaa gaa ata atg gca aat aac ttt tcc ttg gag agt cat 313
Pro Leu Arg Glu Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His
45 50 55 60
25 aac ata toa ctg act gaa cat tct agt atg cca gta gaa aaa aat atc 361
Asn Ile Ser Leu Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile
65 70 75
act tta gaa agg cct tct aat gta aat ctc aca tgc cag ttc aca aca 409
Thr Leu Glu Arg Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr
30 80 85 90
tct ggg gat ttg aat gca gta aat gtg act tgg aaa aaa gat ggt gaa 457
Ser Gly Asp Leu Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu
95 100 105
caa ctt gag aat aat tat ctt gtc agt gca aca gga agc acc ttg tat 505
35 Gln Leu Glu Asn Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr

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	110	115	120	
	acc caa tac agg ttc acc atc att aat agc aaa caa atg gga agt tat			553
	Thr Gln Tyr Arg Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr			
	125	130	135	140
5	tct tgt ttc ttt cga gag gaa aag gaa caa agg gga aca ttt aat ttc			601
	Ser Cys Phe Phe Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe			
	145	150	155	
	aaa gtc cct gaa ctt cat ggg aaa aac aag cca ttg atc tct tac gta			649
	Lys Val Pro Glu Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val			
10	160	165	170	
	ggg gat tct act gtc ttg aca tgt aaa tgt caa aat tgt ttt cct tta			697
	Gly Asp Ser Thr Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu			
	175	180	185	
	aat tgg acc tgg tac agt agt aat ggg agt gta aag gtt cct gtt ggt			745
15	Asn Trp Thr Trp Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly			
	190	195	200	
	gtt caa atg aat aaa tat gtg atc aat gga aca tat gct aac gaa aca			793
	Val Gln Met Asn Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr			
	205	210	215	220
20	aag ctg aag ata aca caa ctt ttg gag gaa gat ggg gaa tct tac tgg			841
	Lys Leu Lys Ile Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp			
	225	230	235	
	tgc cgt gca cta ttc caa tta ggc gag agt gaa gaa cac att gag ctt			889
	Cys Arg Ala Leu Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu			
25	240	245	250	
	gtg gtg ctg agc tat ttg gtg ccc etc aaa cca ttt ctt gta ata gtg			937
	Val Val Leu Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val			
	255	260	265	
	gct gag gtg att ctt tta gtg gcc acc att ctg ctt tgt gaa aag tac			985
30	Ala Glu Val Ile Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr			
	270	275	280	
	aca caa aag aaa aag aag cac tca gat gag ggg aaa gaa ttt gag cag			1033
	Thr Gln Lys Lys Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln			
	285	290	295	300
35	att gaa cag ctg aaa tca gat gat agc aat ggt ata gaa aat aat gtc			1081

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Ile Glu Gln Leu Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val
305 310 315
ccc agg cat aga aaa aat gag tct ctg ggc cag tgaatacaaa acatca 1130
Pro Arg His Arg Lys Asn Glu Ser Leu Gly Gln
5 320 325
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taagagcctc tgagttttta gttttaaaag gatgaaaagc ttatgcaaca tgctcagcag 1250
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cataaaagca atgtaaatca gaataaatat gttagaccag aataaaatta attatattct 1370
10 ggtcttcaaa ggacacacag aacagatata agcagaatca cttaatactt catagaacaa 1430
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Met Lys Phe Val Pro Cys Leu Leu Val Thr Leu Ser Cys Leu
30 1 5 10 15
ggg act ttg ggt cag gcc ccg agg caa aag caa gga agc act ggg gag 154
Gly Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Glu
20 25 30
gaa ttc cat ttc cag act gga ggg aga gat tcc tgc act atg cgt ccc 202
35 Glu Phe His Phe Gln Thr Gly Gly Arg Asp Ser Cys Thr Met Arg Pro

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	35	40	45	
	agc agc ttg ggg caa ggt gct gga gaa gtc tgg ctt cgc gtc gac tgc	250		
	Ser Ser Leu Gly Gln Gly Ala Gly Glu Val Trp Leu Arg Val Asp Cys			
	30	55	60	
5	cgc aac aca gac cag acc tac tgg tgt gag tac agg ggg cag ccc agc	298		
	Arg Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser			
	65	70	75	
	atg tgc cag gct ttc gct gct gac ccc aaa tct tac tgg aat caa gcc	346		
	Met Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala			
10	80	85	90	95
	ctg cag gag ctg agg cgc ctt cac cat gcg tgc cag ggg gcc ccg gtg	394		
	Leu Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val			
	100	105	110	
	ctt agg cca tcc gtg tgc agg gag gct gga ccc cag gcc cat atg cag	442		
15	Leu Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln			
	115	120	125	
	cag gtg act tcc agc ctc aag ggc agc cca gag ccc aac cag cag cct	490		
	Gln Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro			
	130	135	140	
20	gag gct ggg acg cca tct ctg agg ccc aag gcc aca gtg aaa ctc aca	538		
	Glu Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr			
	145	150	155	
	gaa gca aca cag ctg gga aag gac tcg atg gaa gag ctg gga aaa gcc	586		
	Glu Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala			
25	160	165	170	175
	aaa ccc acc acc cga ccc aca gcc aaa cct acc cag cct gga ccc agy	634		
	Lys Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg			
	180	185	190	
	ccc gga ggg aat gag gaa gca aag aag aag gcc tgg gaa cat tgt tgg	682		
30	Pro Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp			
	195	200	205	
	aaa ccc ttc cag gcc ctg tgc gcc ttt ctc atc agc ttc ttc cga ggg	730		
	Lys Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly			
	210	215	220	
35	tgacagggtga aagacccta cagatctgac ctctccctga cagacaacca tctcttttta	790		

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 caacggccca aattcttgat ctgcagcttc tctgaagttt ggaaaagaaa ccttccttcc 910
 tggagtttgc agagttcagc aatatgatag ggaacagggtg ctgatggggc caagagtgcac 970
 aagcatacac aactaactat tatctgtaga agttttgott tgttgatctg agccttctat 1030
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 Met Arg Leu Leu
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 Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser
 5 10 15 20
 gcc aat ctg gcc gcc gtg ccc agc aag aga tta aag atg cag tac gcc 150
 Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala

25 25 30 35
 acg ggg ccg ctg ctc aag ttc cag att tgt gtt tcc tgag 190
 Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser
 40 45

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	Ser Ile Asn Thr	Leu Ser Ala	Lys Trp Ala	Asp Asr Phe	Met Ala Glu		
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	Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu Cys Asp	
	85 90 95	
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	Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr Ser Ala	
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	Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val Ile Thr	
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	Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile Gln Met	
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	Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro Leu Arg	
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	Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser Leu Leu	
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	Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser Ile Ala			
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	Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu His Arg			
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	Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu Glu Ser			
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	gag cag gag aga ctg ctg ggt ggc acc cgc act ooc atc aat gat gcc	1160		
	Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn Asp Ala			
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	agc tgagggtccc tggaggettc taatgccacc cgggtgetcc ttetccc	1210		
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	agtggcagac ctcagctctc tggacccctc ctacagcact agagctaat catgaagtg	1450		
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15	cag tgc cct gag cac agt caa ctg aca act ctg ggc gtg gat ggg aag Gln Cys Pro Glu His Ser Gln Leu Thr Thr Leu Gly Val Asp Gly Lys 25 30 35	150
	gag ttc cca gag gtc cac ttg ggc cag tgg tac ttt atc gca ggg gaa Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr Phe Ile Ala Gly Ala 40 45 50	198
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	gtc ttc aat atg gct gct ggc tct gcc ccg atg cag ctg cac ctt cgt Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met Gln Leu His Leu Arg 70 75 80 85	294
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	Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe	
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	Thr	Thr	Ile	Gly	Tyr	Gly	Asn	Val	Ala	Pro	Lys	Thr	Pro	Ala	Gly	Arg	
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	Leu	Phe	Cys	Val	Phe	Tyr	Gly	Leu	Phe	Gly	Val	Pro	Leu	Cys	Leu	Thr	
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	tgg	atc	agt	gcc	ctg	ggc	aag	ttc	ttc	ggg	gga	cgt	gcc	aag	aga	cta	789
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	Gly	Gln	Phe	Leu	Thr	Lys	Arg	Gly	Val	Ser	Leu	Arg	Lys	Ala	Gln	Ile	
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	Thr	Cys	Thr	Val	Ile	Phe	Ile	Val	Trp	Gly	Val	Leu	Val	His	Leu	Val	
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	atc	cca	ccc	ttc	gta	ttc	atg	gtg	act	gag	ggg	tgg	aac	tac	atc	gag	933
	Ile	Pro	Pro	Phe	Val	Phe	Met	Val	Thr	Glu	Gly	Trp	Asn	Tyr	Ile	Glu	
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	Gly	Leu	Tyr	Tyr	Ser	Phe	Ile	Thr	Ile	Ser	Thr	Ile	Gly	Phe	Gly	Asp	
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	Tyr	Phe	Val	Glu	Leu	Trp	Ile	Tyr	Leu	Gly	Leu	Ala	Trp	Leu	Ser	Leu	
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	Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu	
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	Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser	
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 Val Thr Gly Leu Gly Ile Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr
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 Thr Phe Tyr Ser Ile Ser Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp
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	<213> Homo sapiens	
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	tagaagttgc atctgagaaa gtagccaga agaca atg gac tat gtg tgc tgt	113
	Met Asp Tyr Val Cys Cys	
25	1 5	
	gct tac aac aac ata acc ggc agg caa gat gaa act cat ttc aca gtt	161
	Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp Glu Thr His Phe Thr Val	
	10 15 20	
	atc atc act tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca	209
30	Ile Ile Thr Ser Val Gly Leu Glu Lys Leu Ala Gln Lys Gly Lys Ser	
	25 30 35	
	ttg tca cct tta gca agt ata act gga ata tca cta ttt ttg att ata	257
	Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile Ser Leu Phe Leu Ile Ile	
	40 45 50	
35	tcc atg tgt ctt ctc ttc cta tgg aaa aaa tat caa ccc tac aaa gtt	305

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Ser Met Cys Leu Leu Phe Leu Trp Lys Lys Tyr Gln Pro Tyr Lys Val
 55 60 65 70
 ata aaa cag aaa cta gaa ggc agg cca gaa aca gaa tac agg aaa got 353
 ile Lys Gln Lys Leu Glu Gly Arg Pro Glu Thr Glu Tyr Arg Lys Ala
 5 75 80 85
 caa aca ttt tca ggc cat gaa gat gct ctg gat gac ttc gga ata tat 401
 Gln Thr Phe Ser Gly His Glu Asp Ala Leu Asp Asp Phe Gly Ile Tyr
 90 95 100
 gaa ttt gtt gct ttt cca gat gtt tct ggt gtt tcc agg atc cca agc 449
 10 Glu Phe Val Ala Phe Pro Asp Val Ser Gly Val Ser Arg Ile Pro Ser
 105 110 115
 agg tct gtt cca gcc tct gat tgt gta tct ggg caa gat ttg cac agt 497
 Arg Ser Val Pro Ala Ser Asp Cys Val Ser Gly Gln Asp Leu His Ser
 120 125 130
 15 aca gtg tat gaa gtt att cag cac atc cct gcc cag cag caa gac cat 545
 Thr Val Tyr Glu Val Ile Gln His Ile Pro Ala Gln Gln Gln Asp His
 135 140 145 150
 cca gag tgaactttca tgggctaaac agtacattcg agtgaatttc tgaagaac 600
 Pro Glu
 20
 attttaagga aaaacagtgg aaaagtatat taatctggaa tcagtgaaga aaccaagacc 660
 aacacctctt actcattatt cctttacatg cagaatagag gcatttatgc aaattgaact 720
 gcagggtttt cagcatatac acaatgtctt gtgcaacaga aaacatggtt ggggaaatat 780
 tcttcagtgg agagtcgttc tcatgctgac ggggagaacg aaagtgcag gggtttcttc 840
 25 ataagttttg tatgaatat ctctacaaac ctcaattagt tctactctac actttcaata 900
 tcatcaaacac tgagactatc ctgtctcacc tacaattgtg gaaactttac attgttcgat 960
 ttttcagcag actttgtttt attaaatttt tattagtgtt aagaatgcta aagtttcaat 1020
 tttatttcca aattctatc ttgttatttg tacaacaaag taataaggat ggttgcaca 1080
 aaacaaaaac tatgccttct ctttttttcc aatcaccagt agtatttttg agaagacttg 1140
 30 tgaacactta aggaatgac tattaaagtc ttatttttat ttttttcaag gaaagatgga 1200
 ttcaataaaa ttattctgtt ttgttttt 1229
 <210> 91
 <211> 358
 35 <212> PRT

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<213> Homo sapiens

<400> 91

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          20          25          30
Pro Arg Ser Ala Ser Ile Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu
          35          40          45
10  Ala Leu Gln Leu His Pro Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln
          50          55          60
Glu Lys Phe Gln Asp Leu Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser
          65          70          75          80
Glu Lys Arg Lys Gln Tyr Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp
15          85          90          95
Gly His Gln Ser Ser His Gly Asp Ile Phe Ser His Phe Phe Gly Asp
          100          105          110
Phe Gly Phe Met Phe Gly Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile
          115          120          125
20  Pro Arg Gly Ser Asp Ile Ile Val Asp Leu Glu Val Thr Leu Glu Glu
          130          135          140
Val Tyr Ala Gly Asn Phe Val Glu Val Val Arg Asn Lys Pro Val Ala
          145          150          155          160
Arg Gln Ala Pro Gly Lys Arg Lys Cys Asn Cys Arg Gln Glu Met Arg
25          165          170          175
Thr Thr Gln Leu Gly Pro Gly Arg Phe Gln Met Thr Gln Glu Val Val
          180          185          190
Cys Asp Glu Cys Pro Asn Val Lys Leu Val Asn Glu Glu Arg Thr Leu
          195          200          205
30  Glu Val Glu Ile Glu Pro Gly Val Arg Asp Gly Met Glu Tyr Pro Phe
          210          215          220
Ile Gly Glu Gly Glu Pro His Val Asp Gly Glu Pro Gly Asp Leu Arg
          225          230          235          240
Phe Arg Ile Lys Val Val Lys His Pro Ile Phe Glu Arg Arg Gly Asp
35          245          250          255

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Asp Leu Tyr Thr Asn Val Thr Ile Ser Leu Val Glu Ser Leu Val Gly
 260 265 270
 Phe Glu Met Asp Ile Thr His Leu Asp Gly His Lys Val His Ile Ser
 275 280 285
 5 Arg Asp Lys Ile Thr Arg Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu
 290 295 300
 Gly Leu Pro Asn Phe Asp Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile
 305 310 315 320
 Thr Phe Asp Val Asp Phe Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg
 10 325 330 335
 Glu Gly Ile Lys Gln Leu Leu Lys Gln Gly Ser Val Gln Lys Val Tyr
 340 345 350
 Asn Gly Leu Gln Gly Tyr
 355
 15
 <210> 92
 <211> 226
 <212> PRT
 <213> Homo sapience
 20
 <400> 92
 Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser Asn Ser Cys Cys
 1 5 10 15
 Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr
 25 20 25 30
 Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala
 35 40 45
 Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe
 50 55 60
 30 Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu
 65 70 75 80
 Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln
 85 90 95
 Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe
 25 100 105 110

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Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile Tyr Pro Asn Ser
 115 120 125
 Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe Pro Tyr Arg Asp
 130 135 140
 5 Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu Ile Ile Leu Leu
 145 150 155 160
 Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu Ile Ser Cys Val
 165 170 175
 Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu
 10 180 185 190
 Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Pro Tyr Asp
 195 200 205
 Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro Pro Tyr Val
 210 215 220
 15 Ser Ala
 225

 <210> 93
 <211> 195
 20 <212> PRT
 <213> Homo sapiens

 <400> 93
 Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg
 25 1 5 10 15
 Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys
 20 25 30
 Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser
 35 40 45
 30 Xaa Gly Tyr Arg Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln
 50 55 60
 Arg Tyr Pro Asp Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro
 65 70 75 80
 Ile Tyr Arg His Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu
 35 85 90 95

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Ile Gly Leu Ile Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met
 100 105 110
 Gln Ala Pro Ser Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala
 115 120 125
 5 Cys Met Met Val Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met
 130 135 140
 Ser Thr Gly Ala Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser
 145 150 155 160
 Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile
 10 165 170 175
 Leu Asp Asn Glu Met Lys Leu Asn Val His Met Asp Ser Ile Pro His
 180 185 190
 His Arg Ser
 195
 15
 <210> 94
 <211> 339
 <212> PRT
 <213> Homo sapiance
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 <400> 94
 Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu
 1 5 10 15
 Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu
 25 20 25 30
 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu
 35 40 45
 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu
 50 55 60
 30 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser
 65 70 75 80
 Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu
 85 90 95
 Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu
 35 100 105 110

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Thr Asp Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu
115 120 125
Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg
130 135 140
5 Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu
145 150 155 160
Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His
165 170 175
Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu
10 180 185 190
Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His
195 200 205
Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr
210 215 220
15 Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn
225 230 235 240
Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn
245 250 255
Asn Gly Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu
20 260 265 270
Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu
275 280 285
Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp
290 295 300
25 Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe
305 310 315 320
Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr
325 330 335
Lys His Asp
30
<210> 95
<211> 487
<212> PRT
<213> Homo sapiens
35

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<400> 95

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Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys
  1           5           10          15
Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro
5           20           25           30
Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val
  35           40           45
Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser
  50           55           60
10 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu
  65           70           75           80
Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe
  85           90           95
Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu
15           100          105          110
Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala
  115          120          125
Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser
  130          135          140
20 Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu
  145          150          155          160
Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val
  165          170          175
Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala
25           180          185          190
Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile
  195          200          205
Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile
  210          215          220
30 Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val
  225          230          235          240
Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu
  245          250          255
Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala
35           260          265          270

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Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro
 275 280 285
 Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser
 290 295 300
 5 Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro
 305 310 315 320
 Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg
 325 330 335
 Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu
 10 340 345 350
 Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser
 355 360 365
 Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Val Val Pro
 370 375 380
 15 Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser
 385 390 395 400
 Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu
 405 410 415
 Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu
 20 420 425 430
 Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu
 435 440 445
 Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe
 450 455 460
 25 Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser
 465 470 475 480
 Glu Leu Ala Ser Gly Pro Pro
 485

30 <210> 96
 <211> 393
 <212> PRT
 <213> Homo sapience

35 <400> 96

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Met Arg Thr Leu Phe Asn Leu Leu Trp Leu Ala Leu Ala Cys Ser Pro
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 Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala Ala Ser Lys
 20 25 30
 5 Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp Lys Pro Val Gln Asp Arg
 35 40 45
 Gly Leu Val Val Thr Asp Leu Lys Ala Glu Ser Val Val Leu Glu His
 50 55 60
 Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp Arg His Phe Ala Gly Asp
 10 65 70 75 80
 Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr Asp Val Thr
 85 90 95
 Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val Trp Leu Gln
 100 105 110
 15 Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Val Thr Gly Leu His Asp
 115 120 125
 Val Asp Gln Gly Trp Met Arg Ala Val Arg Lys His Ala Lys Gly Leu
 130 135 140
 His Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr Asp Asp Phe
 20 145 150 155 160
 Arg Asn Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu Ser Lys Thr
 165 170 175
 Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe Val Val Glu
 180 185 190
 25 Val Trp Asn Gln Leu Leu Ser Gln Lys Arg Val Gly Leu Ile His Met
 195 200 205
 Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu Leu Ala Leu
 210 215 220
 Leu Val Ile Pro Pro Ala Ile Thr Pro Gly Thr Asp Gln Leu Gly Met
 30 225 230 235 240
 Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Val Leu Asp Gly Phe
 245 250 255
 Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala His Gln Pro Gly Pro Asn
 260 265 270
 35 Ala Pro Leu Ser Trp Val Arg Ala Cys Val Gln Val Leu Asp Pro Lys

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275 280 285
 Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe Tyr Gly Met
 290 295 300
 Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu Pro Val Val Gly Ala Arg
 5 305 310 315 320
 Tyr Ile Gln Thr Leu Lys Asp His Arg Pro Arg Met Val Trp Asp Ser
 325 330 335
 Gln Ala Ser Glu His Phe Phe Glu Tyr Lys Lys Ser Arg Ser Gly Arg
 340 345 350
 10 His Val Val Phe Tyr Pro Thr Leu Lys Ser Leu Gln Val Arg Leu Glu
 355 360 365
 Leu Ala Arg Glu Leu Gly Val Gly Val Ser Ile Trp Glu Leu Gly Gln
 370 375 380
 Gly Leu Asp Tyr Phe Tyr Asp Leu Leu
 15 385 390

 <210> 97
 <211> 196
 <212> PRT
 20 <213> Homo sapience

 <400> 97
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 25 Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr Leu Ala
 20 25 30
 Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro Gly Gly
 35 40 45
 Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile Thr Gly
 30 50 55 60
 Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln Val Lys
 65 70 75 80
 Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly Asn Thr
 85 90 95
 35 Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val Phe Val

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100 105 110
 Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp
 115 120 125
 Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr
 5 130 135 140
 Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln Tyr Gln
 145 150 155 160
 Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu
 165 170 175
 10 Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala Asn Ser
 180 185 190
 Pro Val Gly Arg
 195
 15 <210> 98
 <211> 107
 <212> PRT
 <213> Homo sapience
 20 <400> 98
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met Ser
 1 5 10 15
 Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly Ser
 20 25 30
 25 Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly Ile
 35 40 45
 Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser
 50 55 60
 Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala
 30 65 70 75 80
 Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser
 85 90 95
 Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro
 100 105
 35

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<210> 99
 <211> 350
 <212> PRT
 <213> Homo sapiens

5

<400> 99

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 10 20 25 30
 Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser
 35 40 45
 Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Gln
 50 55 60
 15 Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln Tyr Gln Leu Leu Lys
 65 70 75 80
 Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser Lys Ile Ser Leu Ile
 85 90 95
 Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met Glu Gln Leu Lys Ser
 20 100 105 110
 Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Glu Glu Ile Asn Glu
 115 120 125
 Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys Gln Asp Ile Leu Asn
 130 135 140
 25 Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser
 145 150 155 160
 Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys
 165 170 175
 Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu
 30 180 185 190
 Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile Glu Lys Val Glu Lys
 195 200 205
 Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser Ser Ser Ile Asp Arg
 210 215 220
 35 Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn Ser Gln Arg Ile Asn

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225 230 235 240
 Ser Val Lys Lys Thr Leu Thr Glu Leu Lys Ser Asp Phe Asp Lys His
 245 250 255
 Thr Asp Arg Phe Leu Ser Leu Glu Gly Asp Arg Ala Lys Val Leu Lys
 5 260 265 270
 Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys Val Tyr Asn Leu Lys
 275 280 285
 Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn Asp Leu Thr Leu Arg
 290 295 300
 10 Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Glu Lys Glu Ile Ala
 305 310 315 320
 Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile Val Gln Ala Glu Ile
 325 330 335
 Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser Asp Met Asn
 15 340 345 350

 <210> 100
 <211> 107
 <212> PRT
 20 <213> Homo sapience

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 25 Thr Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser
 20 25 30
 Ile Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu
 35 40 45
 Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val
 30 50 55 60
 Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu
 65 70 75 80
 Leu Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly
 85 90 95
 35 Arg Pro Ala Gly Gly Ala His Leu Cys Ala Ala

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100

105

<210> 101

<211> 1074

5 <212> DNA

<213> Homo Sapiens

<400> 101

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 attaaaaagg cctataggaa actagccctg cagcttcctc ccgaccggaa ccctgatgat 180
 ccacaagccc agggagaaatt ccaggatctg ggtgctgctt atgaggttct gtcagatagt 240
 gagaacacga aacagtacga tacttatggt gaagaaggat taaaagatgg tcacagagc 300
 tcccatggag acattttttc acacttcttt ggggattttg gtttcatgtt tggaggaaac 360
 15 cctcgtcagc aagacagaaa tattccaaga ggaagtata ttattgtaga tctagaagtc 420
 actttggaag aagtatatgc aggaattttt gtggaagtag ttagaaacaa acctgtggca 480
 aggcaggctc ctggcaaacg gaagtgaat tgcgggcaag agatgcggac caccagctg 540
 ggccctgggc gcttccaaat gaccagagag gtggtctgcg acgaatgcc taatgtcaaa 600
 ctagtgaatg aagaacgaac gctggaagta gaaatagagc ctggggtgag agacggcatg 660
 20 gagtacccct ttattggaga aggtgagcct cactgggatg gggagcctgg agatttacgg 720
 ttccgaatca aagttgtcaa gcacccaata ttgaaagga gaggagatga tttgtacaca 780
 aatgtgacaa tctcattagt tgagtcactg gttggctttg agatggatat tactcacttg 840
 gatggtcaca aggtacatat ttccgggat aagatcacca ggccaggagc gaagctatgg 900
 aagaaagggg aagggtcccc caactttgac aacaacaata tcaagggtc tttgataatc 960
 25 acttttgatg tggattttcc aaaagaacag ttaacagagg aagcgagaga aggtatcaaa 1020
 cagctactga aacaagggtc agtcagaag gtatacaatg gactgcaagg atat 1074

<210> 102

<211> 678

30 <212> DNA

<213> Homo Sapiens

<400> 102

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 35 gtccgcaccc gcaccatcct gctcggcgtc tggatatctg tcatcaatgc tgtggtactg 120

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ttgattttat tgagtgcctt ggctgatccg gatcagtata acttttcaag ttctgaactg 180
 ggaggtgact ttgagttcat ggatgatgcc aacatgtgca ttgccattgc gattttctct 240
 ctcatgatcc tgatatgtgc tatggctact taaggagcgt acaagcaacg cgcagcctgg 300
 atcatcccat tcttctgtta ccagatcttt gactttgccc tgaacatgtt ggttgcaatc 360
 5 actgtgctta tttatccaaa ctccattcag gaatacatac ggcaactgcc tctaattttt 420
 ccctacagag atgatgtcat gtcagtgaat cctacctgtt tggctcctat tattcttctg 480
 tttattagaa ttatcttgac ttttaagggt tacttgatta gctgtgtttg gaactgctac 540
 cgatacatac atggtaggaa ctctctgat gtcctgggtt atgttaccag caatgacaat 600
 acggtgctgc taccctcgta tgatgatgcc actgtgaatg gtgctgocaa ggagccacccg 660
 10 ccaccttacg tgtctgcc 678

<210> 103

<211> 585

<212> DNA

15 <213> Homo Sapiens

<400> 103

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 gccaatctgg gcggcgtgcc cagcaagaga ttaaagatgc agtacgccac ggggcgcgtg 120
 20 ctcaagtcc agatttgtgt ttctgaggt tataggcggg tgtttgagga gtacatgggg 180
 gttattagcc agcggtagcc agacatccgc attgaaggag agaattacct cctcaacca 240
 atatatagac acatagcacc ttctctgtca gtcttcaaac tagtattaat aggccttaata 300
 attgttgcca aggatacctt tgccttcttt ggcatgcaag ctctagcat ctggcagtg 360
 ggccaagaaa ataaggctta tgcattgtat atgggtttct tcttgagcaa catgattgag 420
 25 aaccagtgtg tgcacacagg tgcatttgag ataacttta atgatgtacc tgtgtggtct 480
 aagctggaat ctggtagcct tccatccatg caacaacttg ttcaaatctt tgacaatgaa 540
 atgaagctca atgtgcatat ggattcaatc ccacaccatc gatca 585

<210> 104

30 <211> 1017

<212> DNA

<213> Homo Sapiens

<400> 104

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	tacatocaga cactgaagga ccacaggccc cggatggtgt gggacagcca ggctoagag	1020
	cacttcttcg agtacaagaa gagccgcagt gggaggcacg tcgtcttcta cccaacctg	1080
	aagtcctgc aggtgcggt ggagctggcc cgggagctgg gcgttgggt ctctatctg	1140
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	cttgagagact cctgggacgt gaaactggga gccttaggtg ggaataccca ggaagtcacc	300
	ctgcagccag gcgaatacat cacaagaatc tttgtgcct tccaagcttt cctccggggt	360
	atggtcatgt acaccagca ggaccgat tatctatttg ggaagcttga tggccagatc	420
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<211> 1050

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5 <213> Homo Sapience

<400> 109

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10	gcagacccc gaacgtgcct gagectgctg tcgctgggga cgtgcctggg cctggcctgg	180
	tttgtatttc agcagtcaga aaaatttgca aagggtggaa accaatacca gttactgaaa	240
	ctagaaacca atgaattcca acaacttcaa agtaaaatca gtttaatttc agaaaagtgg	300
	cagaaatctg aagctatcat ggaacaattg aagctcttcc aaataattgc tcacttaag	360
	cgtctacagg aagaatttaa tgaggtaaaa acttgggtcca ataggataac tgaanaacag	420
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	cggatttccg gtttagtaac tgatgtaata tcattgacag attctgtgca agaactagaa	600
	aataaaatag agaaagtaga aaaaaatata gtaaaaaata taggtgatct tctttcaagc	660
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<211> 321

<212> DNA

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<400> 110

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	gaggagtgtg tggaacagga cccgggacag aggaacc atg got cag aac atg	175
	Met Ala Pro Gln Asn Leu	
	1 5	
	agc acc ttt tgc ctg ttg ctg cta tac ctc atc ggg gcg gtg att gcc	223
20	Ser Thr Phe Cys Leu Leu Leu Tyr Leu Ile Gly Ala Val Ile Ala	
	10 15 20	
	gga cga gat ttc tat aag atc ttg ggg gtg cct cga agt gcc tct ata	271
	Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val Pro Arg Ser Ala Ser Ile	
	25 30 35	
25	aag gat att aaa aag gcc tat agg aaa cta gcc ctg cag ctt cat ccc	319
	Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Gln Leu His Pro	
	40 45 50	
	gac cgg aac cct gat gat cca caa gcc cag gag aaa ttc cag gat ctg	367
	Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Glu Lys Phe Gln Asp Leu	
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	ggt gct gct tat gag gtt ctg tca gat agt gag aaa cgg aaa cag tac	415
	Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser Glu Lys Arg Lys Gln Tyr	
	75 80 85	
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35	Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp Gly His Gln Ser Ser His	

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	105	110	115	
5	gga acc cct cgt cag caa gac aga aat att cca aga gga agt gat att			559
	Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile Pro Arg Gly Ser Asp Ile			
	120	125	130	
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	Ile Val Asp Leu Glu Val Thr Leu Glu Glu Val Tyr Ala Gly Asn Phe			
10	135	140	145	150
	gtg gaa gta gtt aga aac aaa cct gtg gca agg cag gct cct ggc aaa			655
	Val Glu Val Val Arg Asn Lys Pro Val Ala Arg Gln Ala Pro Gly Lys			
	155	160	165	
	egg aag tgc aat tgt cgg caa gag atg cgg acc acc cag ctg ggc cct			703
15	Arg Lys Cys Asn Cys Arg Gln Glu Met Arg Thr Thr Gln Leu Gly Pro			
	170	175	180	
	ggg cgc ttc caa atg acc cag gag gtg gtc tgc gac gaa tgc cct aat			751
	Gly Arg Phe Gln Met Thr Gln Glu Val Val Cys Asp Glu Cys Pro Asn			
	185	190	195	
20	gtc aaa cta gtg aat gaa gaa cga acg ctg gaa gta gaa ata gag cct			799
	Val Lys Leu Val Asn Glu Glu Arg Thr Leu Glu Val Glu Ile Glu Pro			
	200	205	210	
	ggg gtg aga gac ggc atg gag tac ccc ttt att gga gaa ggt gag cct			847
	Gly Val Arg Asp Gly Met Glu Tyr Pro Phe Ile Gly Glu Gly Glu Pro			
25	215	220	225	230
	cac gtg gat ggg gag cct gga gat tta cgg ttc cga atc aaa gtt gtc			895
	His Val Asp Gly Glu Pro Gly Asp Leu Arg Phe Arg Ile Lys Val Val			
	235	240	245	
	aag cac cca ata ttt gaa agg aga gga gat gat ttg tac aca aat gtg			943
30	Lys His Pro Ile Phe Glu Arg Arg Gly Asp Asp Leu Tyr Thr Asn Val			
	250	255	260	
	aca atc tca tta gtt gag tca ctg gtt ggc ttt gag atg gat att act			991
	Thr Ile Ser Leu Val Glu Ser Leu Val Gly Phe Glu Met Asp Ile Thr			
	265	270	275	
35	cac ttg gat ggt cac aag gta cat att tcc cgg gat aag atc acc agg			1039

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	His Leu Asp Gly His Lys Val His Ile Ser Arg Asp Lys Ile Thr Arg	
	280 285 290	
	cca gga gcg aag cta tgg aag aaa ggg gaa ggg ctc ccc aac ttt gac	1087
	Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu Gly Leu Pro Asn Phe Asp	
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	aac aac aat atc aag ggc tct ttg ata atc act ttt gat gtg gat ttt	1135
	Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile Thr Phe Asp Val Asp Phe	
	315 320 325	
	cca aaa gaa cag tta aca gag gaa gcg aga gaa ggt atc aaa cag cta	1183
10	Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg Glu Gly Ile Lys Gln Leu	
	330 335 340	
	ctg aaa caa ggg tca gtg cag aag gta tac aat gga ctg caa gga tat	1231
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	Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu	
	15 20 25	
	ggc gtc tgg tat ctg atc atc aat gct gtg gta ctg ttg att tta ttg	385
	Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu	
	30 35 40	
10	agt gcc ctg gct gat ccg gat cag tat aac ttt tca agt tct gaa ctg	433
	Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu	
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	Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile	
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	Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly	
	80 85 90	
20	gcg tac aag caa cgc gca gcc tgg atc atc cca ttc ttc tgt tac cag	577
	Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln	
	95 100 105	
	atc ttt gac ttt gcc ctg aac atg ttg gtt gca atc act gtg ctt att	625
	Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile	
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	Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe	
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	ccc tac aga gat gat gtc atg tca gtg aat cct acc tgt ttg gtc ott	721
	Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu	
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	att att ctt ctg ttt att agc att atc ttg act ttt aag ggt tac ttg	769
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	190	195	200	
5	ccc ccg tat gat gat gcc act gtg aat ggt gct gcc aag gag cca ccg	913		
	Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro			
	205	210	215	220
	cca cct tac gtg tct gcc taagccttca agtgggcgga gctgagggc	960		
	Pro Pro Tyr Val Ser Ala			
10	225			
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<400> 113

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	Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser	
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	Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala	
	25 30 35	
	acg ggg ccg ctg ctc aag ttc cag att tgt gtt tcc tga ggt tat agg	198
15	Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gly Tyr Arg	
	40 45 50	
	cgg gtg ttt gag gag tac atg cgg gtt att agc cag cgg tac cca gac	246
	Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp	
	55 60 65	
20	atc cgc att gaa gga gag aat tac ctc cct caa cca ata tat aga cac	294
	Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro Ile Tyr Arg His	
	70 75 80	
	ata gca tct ttc ctg tca gtc ttc aaa cta gta tta ata gcc tta ata	342
	Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gly Leu Ile	
25	85 90 95 100	
	att gtt gcc aag gat cct ttt gct ttc ttt gcc atg caa gct cct agc	390
	Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met Gln Ala Pro Ser	
	105 110 115	
	atc tgg cag tgg gcc caa gaa aat aag gtt tat gca tgt atg atg gtt	438
30	Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala Cys Met Met Val	
	120 125 130	
	tto ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca	486
	Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met Ser Thr Gly Ala	
	135 140 145	
35	ttt gag ata act tta aat gat gta cct gtg tgg tot aag ctg gaa tct	534

Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser Lys Leu Glu Ser

5	165	170	175	180	
	atg aag ctc aat gtg cat atg gat tca atc cca cac cat cga tca				627
	Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser				

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	Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu Leu	
	5 10 15	
	ttg gtg cag ctg ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta	214
5	Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu	
	20 25 30	
	cta tgg gcc gag tgg cag gga cga cgc cca gaa tgg gag ctg act gat	262
	Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp	
	35 40 45 50	
10	atg gtg gtg tgg gtg act gga gcc tcg agt gga att ggt gag gag ctg	310
	Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu	
	55 60 65	
	gct tac cag ttg tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga	358
	Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg	
15	70 75 80	
	aga gtg cat gag ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc	406
	Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly	
	85 90 95	
	aat tta aaa gaa aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac	454
20	Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp	
	100 105 110	
	act ggt tcc cat gaa gcg gct acc aaa gct gtt etc cag gag ttt ggt	502
	Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu Phe Gly	
	115 120 125 130	
25	aga atc gac att ctg gtc aac aat ggt gga atg tcc cag cgt tct ctg	550
	Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg Ser Leu	
	135 140 145	
	tgo atg gat acc agc ttg gat gtc tac aga aag cta ata gag ctt aac	598
	Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu Leu Asn	
30	150 155 160	
	tac tta ggg acg gtg tcc ttg aca aaa tgt gtt ctg cct cac atg atc	646
	Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile	
	165 170 175	
	gag agg aag caa gga aag att gtt act gtg aat agc atc ctg ggt atc	694
35	Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile	

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	180	185	190	
	ata tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc	742		
	Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu			
	195 200 205 210			
5	cgg ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt	790		
	Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly			
	215 220 225			
	ata ata gtt tct aac att tgc cca gga cct gtg caa tca aat att gtg	838		
	Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val			
10	230 235 240			
	gag aat tcc cta gct gga gaa gtc aca aag agt ata ggc aat aat gga	886		
	Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly			
	245 250 255			
	gac cag tcc cac aag atg aca acc agt cgt tgt gtg cgg ctg atg tta	934		
15	Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu			
	260 265 270			
	atc agc atg gcc aat gat ttg aaa gaa gtt tgg atc tca gaa caa cct	982		
	Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro			
	275 280 285 290			
20	ttc ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg	1030		
	Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp			
	295 300 305			
	tgg ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt	1078		
	Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser			
25	310 315 320			
	ggt gtg gat gca gac tct tct tat ttt aaa atc ttt aag aca aaa cat	1126		
	Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr Lys His			
	325 330 335			
	gac tgaanagagc atctgtactt ttcaagccac tggagggaaa aatggaaaac a	1180		
30	Asp			
	tgaaaacagc aatcttctta tgcttctgaa taatcaaaga ctaatttggt gttttacttt	1240		
	ttaatagata tgactttgct tccaacatgy aatgaaataa aaaataagta at	1292		
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 atg gat ggg aca gag acc cgg cag cgg agg ctg gac agc tgt ggc aag 103
 Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys
 1 5 10 15
 cca ggg gag ctg ggg ctt cct cac ccc ctc agc aca gga gga ctc cct 151
 Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro
 15 20 25 30
 gta gcc tca gaa gat gga gct ctc agg gcc cct gag agc caa agc gtg 199
 Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val
 35 40 45
 acc ccc aag cca ctg gag act gag cct agc agg gag acc gcc tgg tcc 247
 Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser
 20 50 55 60
 ata ggc ctt cag gtg acc gtg ccc ttc atg ttt gca ggc ctg gga ctg 295
 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu
 65 70 75 80
 25 tcc tgg gcc ggc atg ctt ctg gac tat ttc cag cac tgg cct gtg ttt 343
 Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe
 85 90 95
 gtg gag gtg aaa gac ctt ttg aca ttg gtg ccg ccc ctg gtg ggc ctg 391
 Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu
 30 100 105 110
 aag ggg aac ctg gag atg aca ctg gca tcc aga ctc tcc aca gct gcc 439
 Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala
 115 120 125
 aac act gga caa att gat gac ccc cag gag cag cac aga gtc atc agc 487
 35 Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser

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	130	135	140	
	agc aac ctg gcc ctc atc cag gtg cag gcc act gtc gtg ggg ctc ttg			535
	Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu			
	145	150	155	160
5	gct gct gtg gct gcg ctg ctg ttg ggc gtg gtg tct cga gag gaa gtg			583
	Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val			
	165	170	175	
	gat gtc gcc aag gtg gag ttg ctg tgt gcc agc agt gtc ctc act gcc			631
	Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala			
10	180	185	190	
	ttc ctt gca gcc ttt gcc ctg ggg gtg ctg atg gtc tgt ata gtg att			679
	Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile			
	195	200	205	
	ggc gct cga aag ctc ggg gtc aac cca gac aac att gcc acg ccc att			727
15	Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile			
	210	215	220	
	gca gcc agc ctg gga gac ctc atc aca ctg tcc att ctg gct ttg gtt			775
	Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val			
	225	230	235	240
20	agc agc ttc ttc tac aga cac aaa gat agt cgg tat ctg acg ccg ctg			823
	Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu			
	245	250	255	
	gtc tgc ctc agc ttt gcg gct ctg acc cca gtg tgg gtc ctc att gcc			871
	Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala			
25	260	265	270	
	aag cag agc cca ccc atc gtg aag atc ctg aag ttt ggc tgg ttc cca			919
	Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro			
	275	280	285	
	atc atc ctg gcc atg gtc atc agc agt ttc gga gga ctc atc ttg agc			967
30	Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser			
	290	295	300	
	aaa acc gtt tct aaa cag cag tac aaa ggc atg gcg ata ttt acc ccc			1015
	Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro			
	305	310	315	320
35	gtc ata tgt ggt gtt cgt ggc aat ctg gtg gcc att cag acc agc cga			1063

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	Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg	
	325 330 335	
	atc tca acc tac ctg cac atg tgg agt gca cct ggc gtc ctg ccc etc	1111
	Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu	
5	340 345 350	
	cag atg aag aaa ttc tgg ccc aac ccg tgt tct act ttc tgc acg tca	1159
	Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser	
	355 360 365	
	gaa atc aat tcc atg tca gct cga gtc ctg etc ttg ctg gtg gtc cca	1207
10	Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Leu Val Val Pro	
	370 375 380	
	ggc cat ctg att ttc ttc tac atc atc tac ctg gtg gag ggt cag tca	1255
	Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser	
	385 390 395 400	
15	gtc ata aac agc cag acc ttt gtg gtg etc tac ctg ctg gca ggc ctg	1303
	Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu	
	405 410 415	
	atc cag gtg aca atc ctg ctg tac ctg gca gaa gtg atg gtt cgg ctg	1351
	Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu	
20	420 425 430	
	act tgg cac cag gcc ctg gat cct gac aac cac tgc atc ccc tac ctt	1399
	Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu	
	435 440 445	
	aca ggg ctg ggg gac ctg etc ggt act ggc etc ctg gca etc tgc ttt	1447
25	Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe	
	450 455 460	
	ttc act gac tgg cta ctg aag agc aag gca gag ctg ggt ggc atc tca	1495
	Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser	
	465 470 475 480	
30	gaa ctg gca tct gga cct ccc taactgggccc ccgctgggtcc catttgetca ttag	1550
	Glu Leu Ala Ser Gly Pro Pro	
	485	
	aatttcctct caccatcagtg ggatacagaa ttcagtttct cccttgccag gtccttggga	1610
	tggttgaccc ctgcctctgc agtagccttt tgtgagctcg ctaaggtagc tctcacacac	1670
35	ctcggtctcg gggttgatac ctgagcctgc aatagagccc tgaatcaag agcatggctt	1730

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gagtgtgtga atatgatgtg tgcacatget taatgagcgt gcaagtgtgc acacgtttgt 1790
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 ggggtgtgtt gtctttttcc atgcccctgc aacccagatt ggggtggagc aggaaggagc 1910
 tctttctgt tcccaagcct cagaactctt gagctgtggc ttacttctgt tcttcaccag 1970
 5 gtccaagctc cgtggggccac actgtgtgtg tgccaagaag gtgtacagcc tccccaggat 2030
 ggggcctcat acaacccttc atctgcactc aacatttaac cgtgtccttg ctgtcttttt 2090
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 Met Arg Thr Leu Phe Asn Leu Leu Trp Leu
 1 5 10
 gcc ctg gcc tgc agc cct gtt cac act acc ctg tca aag tca gat gcc 158
 Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala
 25 15 20 25
 aaa aaa gcc gcc tca aag acg ctg ctg gag aag agt cag ttt tca gat 203
 Lys Lys Ala Ala Ser Lys Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp
 30 30 35 40
 aag ccg gtg caa gac cgg ggt ttg gtg gtg acg gac ctc aaa gct gag 254
 Lys Pro Val Gln Asp Arg Gly Leu Val Val Thr Asp Leu Lys Ala Glu
 45 50 55
 agt gtg gtt ctt gag cat cgc agc tac tgc tgg gca aag gcc cgg gac 302
 Ser Val Val Leu Glu His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp
 60 65 70
 35 aga cac ttt gct ggg gat gta ctg ggc tat gtc act cca tgg aac agc 350

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	Arg	His	Phe	Ala	Gly	Asp	Val	Leu	Gly	Tyr	Val	Thr	Pro	Trp	Asn	Ser	
	75						80					85					90
	cat	ggc	tac	gat	gtc	acc	aag	gtc	ttt	ggg	agc	aag	ttc	aca	cag	atc	398
	His	Gly	Tyr	Asp	Val	Thr	Lys	Val	Phe	Gly	Ser	Lys	Phe	Thr	Gln	Ile	
5							95					100				105	
	tca	ccc	gtc	tgg	ctg	cag	ctg	aag	aga	cgt	ggc	cgt	gag	atg	ttt	gag	446
	Ser	Pro	Val	Trp	Leu	Gln	Leu	Lys	Arg	Arg	Gly	Arg	Glu	Met	Phe	Glu	
							110					115				120	
	gtc	acg	ggc	ctc	cac	gac	gtg	gac	caa	ggg	tgg	atg	cga	gct	gtc	agg	494
10	Val	Thr	Gly	Leu	His	Asp	Val	Asp	Gln	Gly	Trp	Met	Arg	Ala	Val	Arg	
							125					130				135	
	aag	cat	gcc	aag	ggc	ctg	cac	ata	gtg	cct	cgg	ctc	ctg	ttt	gag	gac	542
	Lys	His	Ala	Lys	Gly	Leu	His	Ile	Val	Pro	Arg	Leu	Leu	Phe	Glu	Asp	
							140					145				150	
15	tgg	act	tac	gat	gat	ttc	cgg	aac	gtc	tta	gac	agt	gag	gat	gag	ata	590
	Trp	Thr	Tyr	Asp	Asp	Phe	Arg	Asn	Val	Leu	Asp	Ser	Glu	Asp	Glu	Ile	
							155					160				170	
	gag	gag	ctg	agc	aag	acc	gtg	gtc	cag	gtg	gca	aag	aac	cag	cat	ttc	638
	Glu	Glu	Leu	Ser	Lys	Thr	Val	Val	Gln	Val	Ala	Lys	Asn	Gln	His	Phe	
20							175					180				185	
	gat	ggc	ttc	gtg	gtg	gag	gtc	tgg	aac	cag	ctg	cta	agc	cag	aag	cgc	686
	Asp	Gly	Phe	Val	Val	Glu	Val	Trp	Asn	Gln	Leu	Leu	Ser	Gln	Lys	Arg	
							190					195				200	
	gtg	ggc	ctc	atc	cac	atg	ctc	acc	cac	ttg	gcc	gag	gct	ctg	cac	cag	734
25	Val	Gly	Leu	Ile	His	Met	Leu	Thr	His	Leu	Ala	Glu	Ala	Leu	His	Gln	
							205					210				215	
	gcc	cgg	ctg	ctg	gcc	ctc	ctg	gtc	atc	ccg	cct	gcc	atc	acc	ccc	ggg	782
	Ala	Arg	Leu	Leu	Ala	Leu	Leu	Val	Ile	Pro	Pro	Ala	Ile	Thr	Pro	Gly	
							220					225				230	
30	acc	gac	cag	ctg	ggc	atg	ttc	acg	cac	aag	gag	ttt	gag	cag	ctg	gcc	830
	Thr	Asp	Gln	Leu	Gly	Met	Phe	Thr	His	Lys	Glu	Phe	Glu	Gln	Leu	Ala	
							235					240				245	
	ccc	gtg	ctg	gat	ggg	ttc	agc	ctc	atg	acc	tac	gac	tac	tct	aca	gcg	878
	Pro	Val	Leu	Asp	Gly	Phe	Ser	Leu	Met	Thr	Tyr	Asp	Tyr	Ser	Thr	Ala	
35							255					260				265	

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	His Gln Pro Gly Pro Asn Ala Pro Leu Ser Trp Val Arg Ala Cys Val	
	270 275 280	
	cag gtc ctg gac cag aag tcc aag tgg cga agc aaa atc ctc ctg ggg	974
5	Gln Val Leu Asp Pro Lys Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly	
	285 290 295	
	ctc aac ttc tat ggt atg gac tac gcg acc tcc aag gat gcc cgt gag	1022
	Leu Asn Phe Tyr Gly Met Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu	
	300 305 310	
10	cct gtt gtc ggg gcc agg tac atc cag aca ctg aag gac cac agg ccc	1070
	Pro Val Val Gly Ala Arg Tyr Ile Gln Thr Leu Lys Asp His Arg Pro	
	315 320 325 330	
	cgg atg gtg tgg gac agc cag gcc tca gag cac ttc ttc gag tac aag	1118
	Arg Met Val Trp Asp Ser Gln Ala Ser Glu His Phe Phe Glu Tyr Lys	
15	335 340 345	
	aag agc cgc agt ggg agg cac gtc gtc ttc tac cca acc ctg aag tcc	1166
	Lys Ser Arg Ser Gly Arg His Val Val Phe Tyr Pro Thr Leu Lys Ser	
	350 355 360	
	ctg cag gtg cgg ctg gag ctg gcc cgg gag ctg ggc gtt ggg gtc tot	1214
20	Leu Gln Val Arg Leu Glu Leu Ala Arg Glu Leu Gly Val Gly Val Ser	
	365 370 375	
	atc tgg gag ctg ggc cag gcc ctg gac tac ttc tac gac ctg ctc t	1260
	Ile Trp Glu Leu Gly Gln Gly Leu Asp Tyr Phe Tyr Asp Leu Leu	
	380 385 390	
25	aggtgggcat tgcggcctcc gcggtggacg tggtcttttc taagccatgg agtgagtgag	1320
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	Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr
	15 20 25 30
	ctt gcc ctc ctg ggg ggc ccc acc tgg gca ggg aag atg tat ggc cot 145
	Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro
10	35 40 45
	gga gga ggc aag tat ttc agc acc act gaa gac tac gac cat gaa atc 193
	Gly Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile
	50 55 60
	aca ggg ctg cgg gtg tct gta ggt ctt ctc ctg gtg aaa agt gtc cag 241
15	Thr Gly Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln
	65 70 75
	gtg aaa ctt gga gac tcc tgg gac gtg aaa ctg gga gcc tta ggt ggg 289
	Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly
	80 85 90
20	aat acc cag gaa gtc acc ctg cag cca ggc gaa tac atc aca aaa gtc 337
	Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val
	95 100 105 110
	ttt gtc gcc ttc caa gct ttc ctc cgg ggt atg gtc atg tac acc agc 385
	Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser
25	115 120 125
	aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct 433
	Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser
	130 135 140
	gcc tac ccc agc caa gag ggg cag gtg ctg gtg ggc atc tat ggc cag 481
30	Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln
	145 150 155
	tat caa ctc ctt ggc atc aag agc att ggc ttt gaa tgg aat tat cca 529
	Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro
	160 165 170
35	cta gag gag ccg acc act gag cca cca gtt aat ctc aca tac tca gca 577

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Leu Glu Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala
 175 180 185 190
 aac tca ccc gtg ggt cgc taggggtggg tatggggcca tccgagctga ggcca 630
 Asn Ser Pro Val Gly Arg
 5 195
 tctgtgtggt ggtggctgat ggtactggag taactgagtc gggacgctga atctgaatcc 690
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 ggcagcgcctt ggccaggccg aaaggacttt ggggtgggg gctgggagtc cgtgtctega 120
 20 atgagggagg agaggtggag ttgccggggc tcaggcccg cctcgagcat ggcggatga 180
 gaggagtcgg gagccgaggc ctagggtcct tcgggtgagg ggagacggag ccagcgagga 240
 g atg gag cag aag ctt gtg gag gag att ctt caa gca atc act atg 286
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met
 1 5 10 15
 25 tca aca gac aca ggt gtt tcc ctt cct tca tat gag gaa gat cag gga 334
 Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly
 20 25 30
 tca aaa etc att cga aaa gct aaa gag gca cca ttc gta ccc gtt gga 382
 Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly
 30 35 40 45
 ata gcg ggt ttt gca gca att gtt gca tat gga tta tat aaa ctg aag 430
 Ile Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys
 50 55 60
 agc agg gga aat act aaa atg tcc att cat ctg atc cac atg cgt gtg 478
 25 Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val

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	65	70	75	
	gca gcc caa ggc ttt gtt gta gga gca atg act gtt ggt atg ggc tat			526
	Ala Ala Gln Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr			
	80	85	90	95
5	tcc atg tat cgg gaa ttc tgg gca aaa cct aag cct tagaagaa			570
	Ser Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro			
	100	105		
	gagatgctgt cttggtcttg ttggaggagc ttgctttagt tagatgtctt attattaaag			630
	ttacctatta ttgtggaaa t			651
10	<210> 119			
	<211> 1310			
	<212> DNA			
	<213> Homo Sapience			
15	<220>			
	<221> CDS			
	<222> (78)...(1130)			
	<400> 119			
20	cgaacgccaa ggcggccacg tctgtctccc cctggtgaag aagctgccct gggtctgtcg			60
	tcttagggtc tccagac atg tct gag gtg aag agc cgg aag aag tgg ggg			110
	Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly			
	1	5	10	
	ccc aag gga gcc cct ggt gcg gag ccc ggg aag cgg agc gag ggc ggg			158
25	Pro Lys Gly Ala Pro Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Gly			
	15	20	25	
	aag acc ccc gtg gcc cgg agc agc gga ggc ggg ggc tgg gca gac ccc			206
	Lys Thr Pro Val Ala Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro			
	30	35	40	
30	cga acg tgc ctg agc ctg ctg tgg ctg ggg acg tgc ctg ggc ctg gcc			254
	Arg Thr Cys Leu Ser Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala			
	45	50	55	
	tgg ttt gta ttt cag cag tca gaa aaa ttt gca aag gtg gaa aac caa			302
	Trp Phe Val Phe Gln Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln			
35	60	65	70	75

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	tac cag tta ctg aaa cta gaa acc aat gaa ttc caa caa ctt caa agt	350
	Tyr Gln Leu Leu Lys Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser	
	80 85 90	
	aaa atc agt tta att tca gaa aag tgg cag aaa tct gaa gct atc atg	398
5	Lys Ile Ser Leu Ile Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met	
	95 100 105	
	gaa caa ttg aag tct ttt caa ata att gct cat cta aag cgt cta cag	446
	Glu Gln Leu Lys Ser Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln	
	110 115 120	
10	gaa gaa att aat gag gta aaa act tgg tcc aat agg ata act gaa aaa	494
	Glu Glu Ile Asn Glu Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys	
	125 130 135	
	cag gat ata ctg aac aac agt ctg acg acg ctt tct caa gac att aca	542
	Gln Asp Ile Leu Asn Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr	
15	140 145 150 155	
	aaa gta gac caa agt aca act tcc atg gca aaa gat gtt ggt ctc aag	590
	Lys Val Asp Gln Ser Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys	
	160 165 170	
	att aca agt gta aaa aca gat ata cga cgg att tca ggt tta gta act	638
20	Ile Thr Ser Val Lys Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr	
	175 180 185	
	gat gta ata tca ttg aca gat tct gtg caa gaa cta gaa aat aaa ata	686
	Asp Val Ile Ser Leu Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile	
	190 195 200	
25	gag aaa gta gaa aaa aat aca gta aaa aat ata ggt gat ctt ctt tca	734
	Glu Lys Val Glu Lys Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser	
	205 210 215	
	agc agt att gat cga aca gca acg ctc cga aag aca gca tct gaa aat	782
	Ser Ser Ile Asp Arg Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn	
30	220 225 230 235	
	tca caa aga att aac tct gtt aag aag acg cta acc gaa cta aag agt	830
	Ser Gln Arg Ile Asn Ser Val Lys Lys Thr Leu Thr Glu Leu Lys Ser	
	240 245 250	
	gac ttc gac aaa cat aca gat aga ttt cta agc tta gaa ggt gac aga	878
35	Asp Phe Asp Lys His Thr Asp Arg Phe Leu Ser Leu Glu Gly Asp Arg	

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	255	260	265	
	gcc aaa gtt ctg aag aca gtg act ttt gca aat gat cta aaa cca aag	926		
	Ala Lys Val Leu Lys Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys			
	270	275	280	
5	gtg tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat	974		
	Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn			
	285	290	295	
	gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta caa aga	1022		
	Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg			
10	300	305	310	315
	gag aaa gaa att gct ttc tta agt gaa aaa ata tct aat tta aca ata	1070		
	Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile			
	320	325	330	
	gtc caa gct gag att aag gat att aaa gat gaa ata gca cac att tca	1118		
15	Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser			
	335	340	345	
	gat atg aat tagtttgaca ttattgagat tagactaagg taattttttt aat	1170		
	Asp Met Asn			
	350			
20	gggacctctc atgagaagac tggtaaatca aaaataatga tattttggag caaaagtcat	1230		
	tttatattta atcctatttt gtacagtata aataaaactt taaaacaggt tgattttcca	1290		
	aaataaatat gctaaaacct	1310		
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25	<211> 1400			
	<212> DNA			
	<213> Homo Sapiens			
	<220>			
	<221> CDS			
30	<222> (233)...(556)			
	<400> 120			
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	tgtaagccgc cccccccc ccataatgcag atttactcgg catggtatg gccagettct	120		
35	aacacagctg gtatttcaag tctcctggga cctcactcag gaatgatacc cctcagtag	180		

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	aagcagcagg tgatcttaac tctttcaaa gagcaggcct gtctgggaag cc atg	235
	Met	
	1	
	tcc tca gca ggc aca gca acc cct ctg gaa atg gat cac aaa ctc act	283
5	Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu Thr	
	5 10 15	
	tct cag cca ggc agg cca agc ttc tat tgt aac agt agg cac agt ata	331
	Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser Ile	
	20 25 30	
10	gtc gga tca tca cat cag ctg ggt ttt tgg ttt agt cat cta gag tcg	379
	Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu Ser	
	35 40 45	
	tct gga cta aag gtc ttt cag gtc tcc ttg ccc tgt gag tgc gtg aac	427
	Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val Asn	
15	50 55 60 65	
	ctc ccc acc oga att gcc tca gtt gtc ctg agc ctc atg tct ctc ctg	475
	Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu Leu	
	70 75 80	
	gtg gtg ggc cag gcc cct gca tgg gaa ggg agc ctg ctg cgg ggc agg	523
20	Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly Arg	
	85 90 95	
	cca gct ggg ggt gct cac cta tgc gca gca tgaagttatt gaaggac	570
	Pro Ala Gly Gly Ala His Leu Cys Ala Ala	
	100 105	
25	tggttggtga tggtggtgag cgtatccttc atggccagcg cgaagtgggc caggtcagcc	630
	aggtgctgcc agcgtctctct ctgggacttg tcttctctgtg ccaggggacc gtggagaaag	690
	tgtcaggggc cgtcactgc agcagcctgc tetgctgcct tccctggcag tggtctgggg	750
	gtggattccc tacacctaga tgtcaaggc cttaactttc ctcccacaaa ggagtcgcag	810
	ccaogctage tetgacttgc cactgtgaca aagttcagct agcagggteta ggcaangact	870
30	gggcaattga gcagaggaga cggacctgtg agtctgacca cgaggcggac cccttcacct	930
	tggtggggc tggctcctggt ccttaggttt tgtcagggtg tccttggttg gatccctcaa	990
	ctaggtgata agcactggag ggggatgacc cgccttggaac gtgtttcttt aacctcctc	1050
	atataatagg gccgtgggat ggtttagag gtaaacgagg atgatggtgt ttaagacca	1110
	gagcttggga ccagggtcc tacacctaat tttctctcct ggtagctgaa caaaggctca	1170
35	aattagctta acaaaagaac aggtgcctg cagccagagt tetgaaggcc atgctttcag	1230

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tttccttgt tgacaattgc tctccagttc ctatgaaagc acagagcctt agggggcctg 1290
gccacagaac acaaccatct taggcctgag ctgtgaacag caggggggttg tgtgtctgtt 1350
ctgtttctct gcttgccgaa cttttcgaat aaaccctatt tcttatttat 1400

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5  <210> 121
    <211> 483
    <212> PRT
    <213> Homo sapience

10 <400> 121
    Met Lys Ala Phe His Thr Phe Cys Val Val Leu Leu Val Phe Gly Ser
      1             5             10             15
    Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile Val
      20             25             30
15  Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp
      35             40             45
    Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu
      50             55             60
    Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly
20  65             70             75             80
    Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro
      85             90             95
    Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser
      100            105            110
25  Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His
      115            120            125
    Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr
      130            135            140
    Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn
30  145            150            155            160
    Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu
      165            170            175
    Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr
      180            185            190
35  Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp

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	195	200	205
	Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg Phe		
	210	215	220
	Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg Pro		
5	225	230	235
	Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp Met		
	245	250	255
	Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg Leu		
	260	265	270
10	Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro Lys		
	275	280	285
	Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser Glu		
	290	295	300
	Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe		
15	305	310	315
	Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp Gln		
	325	330	335
	Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys Leu		
	340	345	350
20	Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser		
	355	360	365
	Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met Asn		
	370	375	380
	Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn Arg		
25	385	390	395
	Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu Asn		
	405	410	415
	Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser Arg		
	420	425	430
30	Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu Glu		
	435	440	445
	Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg Glu		
	450	455	460
	Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys Val		
35	465	470	475
			480

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Lys Ala Met

<210> 122

<211> 334

5 <212> PRT

<213> Homo sapiens

<400> 122

Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg Arg Leu Gln
 10 1 5 10 15
 Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu
 20 25 30
 Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu
 35 40 45
 15 Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro
 50 55 60
 Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp
 65 70 75 80
 Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu
 20 85 90 95
 Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val
 100 105 110
 Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe
 115 120 125
 25 Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu
 130 135 140
 Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu
 145 150 155 160
 Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly
 30 165 170 175
 Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu
 180 185 190
 Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn Arg Lys Gly
 195 200 205
 35 Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe

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210 215 220
 Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn Ser Ser Gly
 225 230 235 240
 Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile
 5 245 250 255
 Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly
 260 265 270
 Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile
 275 280 285
 10 Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val Asn Gln Leu
 290 295 300
 His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu Ala His Lys
 305 310 315 320
 Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe Cys
 15 325 330

 <210> 123
 <211> 267
 <212> PRT
 20 <213> Homo sapience

 <400> 123
 Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly
 1 5 10 15
 25 His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu Phe Leu His Asp
 20 25 30
 Thr Glu Leu Arg Gln Trp Glu Glu Gln Gly Glu Leu Leu Leu Pro Leu
 35 40 45
 Thr Phe Leu Leu Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val
 30 50 55 60
 Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Glu
 65 70 75 80
 Glu Leu Lys Glu Glu Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu
 85 90 95
 35 Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His

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	100	105	110
	Cys Arg Glu Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro		
	115	120	125
	Trp Met Glu Asn Cys Val Gly Glu Arg Asn His Pro Leu Phe Val Val		
5	130	135	140
	Tyr Leu Ala Leu Gln Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala		
	145	150	155
	160		
	Trp Ser Gly Leu Arg Phe Phe Gln Pro Trp Gly Leu Trp Leu Arg Ser		
	165	170	175
10	Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Leu Ser Leu Phe Ser Leu		
	180	185	190
	Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn		
	195	200	205
	Thr Thr Thr Trp Glu Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg		
15	210	215	220
	Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala		
	225	230	235
	240		
	His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Glu Thr Leu Trp Ala		
	245	250	255
20	Glu Glu Glu Glu Glu Gly Ser Ser Pro Ala Val		
	260	265	
	<210> 124		
	<211> 106		
25	<212> PRT		
	<213> Homo sapience		
	<400> 124		
	Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu		
30	1	5	10
	15		
	Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala Leu Asp Asp Pro		
	20	25	30
	Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly		
	35	40	45
35	Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser		

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50 55 60
 Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met
 65 70 75 80
 Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu
 5 85 90 95
 Gln Asn Pro Gln Pro Met Thr Pro Pro Trp
 100 105

 <210> 125
 10 <211> 224
 <212> PRT
 <213> Homo sapiens

 <400> 125
 15 Met Thr Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro
 1 5 10 15
 Tyr Phe Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe
 20 20 25 30
 Trp Lys Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys
 20 35 40 45
 Lys Met Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile
 50 55 60
 Tyr Asp Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp
 65 70 75 80
 25 Leu Ile Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu
 85 90 95
 Tyr Lys Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile
 100 105 110
 Met Ser Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe
 30 115 120 125
 Asp Trp Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val
 130 135 140
 His Tyr Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp
 145 150 155 160
 35 Leu Tyr His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser

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165 170 175
 Val Tyr Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu
 180 185 190
 Gly Ser Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu
 5 195 200 205
 Ala Leu Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser
 210 215 220

 <210> 126
 10 <211> 258
 <212> PRT
 <213> Homo sapiens

 <400> 126
 15 Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val Tyr Ser Val Pro Arg
 1 5 10 15
 Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu Leu Ser Ala Leu Leu
 20 25 30
 Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro Pro Leu Cys His Gly
 20 35 40 45
 Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys Asp Phe Asp Trp Arg
 50 55 60
 Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile Val Met Met Lys Asn
 65 70 75 80
 25 Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly
 85 90 95
 Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu
 100 105 110
 Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp
 30 115 120 125
 Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu
 130 135 140
 Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg
 145 150 155 160
 35 Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr

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165 170 175
 Lys Gln Leu Pro Thr Leu Ile Leu Phe Gln Gly Gly Lys Glu Ala Met
 180 185 190
 Arg Arg Pro Gln Ile Asp Lys Lys Gly Arg Ala Val Ser Trp Thr Phe
 5 195 200 205
 Ser Glu Glu Asn Val Ile Arg Glu Phe Asn Leu Asn Glu Leu Tyr Gln
 210 215 220
 Arg Ala Lys Lys Leu Ser Lys Ala Gly Asp Asn Ile Pro Glu Glu Gln
 225 230 235 240
 10 Pro Val Ala Ser Thr Pro Thr Thr Val Ser Asp Gly Glu Asn Lys Lys
 245 250 255
 Asp Lys

 <210> 127
 15 <211> 110
 <212> PRT
 <213> Homo sapiens

 <400> 127
 20 Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro Pro Phe Ile Ser Glu
 1 5 10 15
 Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser
 20 25 30
 Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly
 25 35 40 45
 Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Leu Ser Leu
 50 55 60
 Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn Lys Tyr Phe Lys Ser
 65 70 75 80
 30 Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly Gly Leu Phe Thr Tyr
 85 90 95
 Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr
 100 105 110

 35 <210> 129

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<211> 91

<212> PRT

<213> Homo sapiens

5

<400> 128

Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser

1 5 10 15

Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu

20 25 30

10

Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys

35 40 45

Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp Gly Arg

50 55 60

Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu

15

65 70 75 80

Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly

85 90

<210> 129

20

<211> 344

<212> PRT

<213> Homo sapiens

<400> 129

25

Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser

1 5 10 15

Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu

20 25 30

Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val

30

35 40 45

Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys

50 55 60

Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe

65 70 75 80

35

Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu

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	85	90	95
	Leu Gly Ser Trp Val Leu Ser Ala	Leu Phe Asp Phe Leu Leu Ile Glu	
	100	105	110
5	Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser		
	115	120	125
	Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser		
	130	135	140
	Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr		
	145	150	155
10	Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly		
	165	170	175
	Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys		
	180	185	190
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser		
15	195	200	205
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser		
	210	215	220
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp		
	225	230	235
20	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe		
	245	250	255
	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met		
	260	265	270
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val		
25	275	280	285
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu		
	290	295	300
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg		
	305	310	315
30	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val		
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<211> 428

<212> PRT

<213> Homo sapiens

5 <400> 130

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 20 25 30
 10 Ala Pro Gly Ser Arg Gly Ala Glu Ala Val Trp Thr Ala Tyr Leu Asn
 35 40 45
 Val Ser Trp Arg Val Pro His Thr Gly Val Asn Arg Thr Val Trp Glu
 50 55 60
 Leu Ser Glu Glu Gly Val Tyr Gly Gln Asp Ser Pro Leu Glu Pro Val
 15 65 70 75 80
 Ala Gly Val Leu Val Pro Pro Asp Gly Pro Gly Ala Leu Asn Ala Cys
 85 90 95
 Asn Pro His Thr Asn Phe Thr Val Pro Thr Val Trp Gly Ser Thr Val
 100 105 110
 20 Gln Val Ser Trp Leu Ala Leu Ile Gln Arg Gly Gly Gly Cys Thr Phe
 115 120 125
 Ala Asp Lys Ile His Leu Ala Tyr Glu Arg Gly Ala Ser Gly Ala Val
 130 135 140
 Ile Phe Asn Phe Pro Gly Thr Arg Asn Glu Val Ile Pro Met Ser His
 145 150 155 160
 25 Pro Gly Ala Val Asp Ile Val Ala Ile Met Ile Gly Asn Leu Lys Gly
 165 170 175
 Thr Lys Ile Leu Gln Ser Ile Gln Arg Gly Ile Gln Val Thr Met Val
 180 185 190
 30 Ile Glu Val Gly Lys Lys His Gly Pro Trp Val Asn His Tyr Ser Ile
 195 200 205
 Phe Phe Val Ser Val Ser Phe Phe Ile Ile Thr Ala Ala Thr Val Gly
 210 215 220
 Tyr Phe Ile Phe Tyr Ser Ala Arg Arg Leu Arg Asn Ala Arg Ala Gln
 35 225 230 235 240

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Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Ala Ile Gly
 245 250 255
 Arg Leu Gln Leu Arg Thr Leu Lys Gln Gly Asp Lys Glu Ile Gly Pro
 260 265 270
 5 Asp Gly Asp Ser Cys Ala Val Cys Ile Glu Leu Tyr Lys Pro Asn Asp
 275 280 285
 Leu Val Arg Ile Leu Thr Cys Asn His Ile Phe His Lys Thr Cys Val
 290 295 300
 Asp Pro Trp Leu Leu Glu His Arg Thr Cys Pro Met Cys Lys Cys Asp
 10 305 310 315 320
 Ile Leu Lys Ala Leu Gly Ile Glu Val Asp Val Glu Asp Gly Ser Val
 325 330 335
 Ser Leu Gln Val Pro Val Ser Asn Glu Ile Ser Asn Ser Ala Ser Ser
 340 345 350
 15 His Glu Glu Asp Asn Arg Ser Glu Thr Ala Ser Ser Gly Tyr Ala Ser
 355 360 365
 Val Gln Gly Thr Asp Glu Pro Pro Leu Glu Glu His Val Gln Ser Thr
 370 375 380
 Asn Glu Ser Leu Gln Leu Val Asn His Glu Ala Asn Ser Val Ala Val
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 gaatttgagg atgtcatgga agactctgtt actgaatctc ctcaacgggt cataatcact 180
 35 gaagatgatg aagatgagac cactgtggag ttggaagggc aggatgaaaa ccaagaagga 240

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	acgattgttg atgttctctg acacctccag aacagctggg agagtatta tctagaaatt	420
	ttgatgggga ctggtctctg tcttatata atgaattaca tcattgggaa gaataaaac	480
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	ttagtggggg atgatggaac taacaaagaa gccacaagca caggaaagtt gaaccaggag	600
	aatgagcaca tctataacct gtggtgttct ggtcagagtgt gctgtgaggg catgcttate	660
	cagctgaggt tctccaagag acaagactta ctgaatgtcc tggcccggat gatgaggcca	720
	gtgagtgatc aagtgcacaa aaaagtaacc atgaatgatg aagacatgga tacctacgta	780
10	tttgcgttg gcacacggaa agccttggtg cgactacaga aagagatgca ggatttgagt	840
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	ccctgatga acatggtgat ttattctatt gataaagcca aaaagttccg actcaacaga	1200
	gaagggcaac aaaaagcaga taagaaccgt gcccgagtag aagagaactt cttgaactg	1260
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	aaggagcgaa tcatgaatga ggaagatcct gagaacacgc gcaggctgga ggaggctgca	1380
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	<211> 1002	
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	ctcctgttta caagattctg gctcctcact gtctgtatg cggcctggtg gtatctggac	180
	cgagacaagc cacggcaggg gggccggcac atccaggcca tcagggtctg gactatatgg	240
	aagtacatga aggaactatt ccccatctcg ctggtcaaga ctgctgagct ggacccctct	300
	cggaaactaca ttgcgggctt ccaaccccat ggagtcctgg cagtcggagc ctttgcacac	360
35	ctgtgcactg agagcacagg cttctctctg atcttccccc gtatccgccc ccactctgatg	420

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 gtcacatcag aaaaggagag tctgtctcac attctgaaca ggaagggttg cggaaacttg 540
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 ctgttactgc ggaaccgaaa gggcttcgtc aggtctgccc tgacacacgg ggcacctctg 660
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<211> 801

<212> DNA

15 <213> Homo sapiens

<400> 133

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 20 caggggggag tgcctctgac cctcacttc ctgctcttg tctgggctc cctgtgtctc 180
 taactgctg tgcactcat ggacctggc taagtgaatg tgcagcccca gctcaggag 240
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 taactgctgg tctgtcagcc cctgagggtt cggactgccc gtgagtgcg ccgttgctgc 360
 cgcgctacg accaccactg cccctggatg gagaactgtg tgggagagcg caaccacca 420
 25 ctctttgtgg tctacctggc gctgcagctg gtgtgtcttc tctggggcct gtacctggca 480
 tggtcaggcc tccggttctt ccagccctgg ggtctgtgtt tgcggctcag cgggtctctg 540
 ttgcacacct tctgtgtgt gtccctcttc tctgtgtgg ccagctgct cctgtctctg 600
 caactctacc tggtyggcag caacaccacc acctgggaat tcatctctc acaccgctc 660
 gcttatctcc gccagcgccc cagcaacccc ttcgaccgag gctgacccg caacctggcc 720
 30 cactttctct gtggatggcc ctcagggtcc tgggagaccc tctgggctga ggaggaggaa 780
 gagggcagca gccagctgt t 801

<210> 134

<211> 318

35 <212> DNA

153/177

<213> Homo sapiens

<400> 134

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 ggcatgaccc tcagcatgtg cggcctcatg cttaaagtga agtgggtggtc ttgggtcgtc 180
 gtctactgct ccttcacag ctttgccaac tctcggagct cggaggacac gaagcaaatg 240
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10

<210> 135

<211> 672

<212> DNA

<213> Homo sapiens

15

<400> 135

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 acctacctct ttgtccaaact ctgcaagatg ctgttcttgg ccactttctt tcccacctgg 180
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 25 ctgtaccaca ccttccggcc agctgtctc ctgtgatgt tctcagtggt ctacaaggcc 540
 ttgtttatgg agacctctgt ccacctctgc tcgtgggca gttgggcagc tctactggcc 600
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30

<210> 136

<211> 774

<212> DNA

<213> Homo sapiens

35

<400> 136

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	aagtacttca atgataaac cattgatgag gaactagaac gggacaagag ggtcacttgg	360
	attgtggagt tctttgcaa ttggtctaat gactgccaat catttgcctc tatctatgct	420
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	tatactgatg ttagtaacgc gtacaaagtg agcacatcac cctcaccaa gcaactccct	540
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	gccggcatcc tcggcctcac cggcctctac ggttctatct tctacctgct cgcctcgtc	180
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	<211> 273	
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35	tctttgataa cagaattctt ctggggaata gctgagtttg tggttttgtt tttcaaaact	120

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<212> DNA
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ttttactgct ccataccaag agtccaagtg gcacaaatto tgggtccgtt gtccatcaca 480
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20 attgtagcca taagtggact tatgtccggg ctgtgtctacg acagcaaaat gttccaggtg 600
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35 <400> 140

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 ccgggtgcag tagacattgt tgcaatcatg atcggcaatc tgaaaggcac aaaaattctg 540
 10 caatctatcc aaagaggcat acaagtaca atggtcatag aagtaggaa aaaacatggc 600
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 35 a atg aaa gcc ttc cac act ttc tgt gtt gtc ctt ctg gtg ttt ggg 166

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	agt	gtc	tct	gaa	gcc	aag	ttt	gat	gat	ttt	gag	gat	gag	gag	gac	ata	214
	Ser	Val	Ser	Glu	Ala	Lys	Phe	Asp	Asp	Phe	Glu	Asp	Glu	Glu	Asp	Ile	
5						20				25					30		
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	Val	Glu	Tyr	Asp	Asp	Asn	Asp	Phe	Ala	Glu	Phe	Glu	Asp	Val	Met	Glu	
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	gac	tct	gtt	act	gaa	tct	cct	caa	cgg	gtc	ata	atc	act	gaa	gat	gat	310
10	Asp	Ser	Val	Thr	Glu	Ser	Pro	Gln	Arg	Val	Ile	Ile	Thr	Glu	Asp	Asp	
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	gaa	gat	gag	acc	act	ctg	gag	ttg	gaa	ggg	cag	gat	gaa	aac	caa	gaa	358
	Glu	Asp	Glu	Thr	Thr	Val	Glu	Leu	Glu	Gly	Gln	Asp	Glu	Asn	Gln	Glu	
						65				70					75		
15	gga	gat	ttt	gaa	gat	gca	gat	acc	cag	gag	gga	gat	act	gag	agt	gaa	406
	Gly	Asp	Phe	Glu	Asp	Ala	Asp	Thr	Gln	Glu	Gly	Asp	Thr	Glu	Ser	Glu	
						80				85					90		
	cca	tat	gat	gat	gaa	gaa	ttt	gaa	ggt	tat	gaa	gac	aaa	cca	gat	act	454
	Pro	Tyr	Asp	Asp	Glu	Glu	Phe	Glu	Gly	Tyr	Glu	Asp	Lys	Pro	Asp	Thr	
20						100				105					110		
	tct	tct	agc	aaa	aat	aaa	gac	cca	ata	acg	att	gtt	gat	gtt	cct	gca	502
	Ser	Ser	Ser	Lys	Asn	Lys	Asp	Pro	Ile	Thr	Ile	Val	Asp	Val	Pro	Ala	
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25	His	Leu	Gln	Asn	Ser	Trp	Glu	Ser	Tyr	Tyr	Leu	Glu	Ile	Leu	Met	Val	
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	Thr	Gly	Leu	Leu	Ala	Tyr	Ile	Met	Asn	Tyr	Ile	Ile	Gly	Lys	Asn	Lys	
						145				150					155		
30	aac	agt	cgc	ctt	gca	cag	gcc	tgg	ttt	aac	act	cat	agg	gag	ctt	ttg	646
	Asn	Ser	Arg	Leu	Ala	Gln	Ala	Trp	Phe	Asn	Thr	His	Arg	Glu	Leu	Leu	
						160				165					170		
	gag	agc	aac	ttt	act	tta	gtg	ggg	gat	gat	gga	act	aac	aaa	gaa	gcc	694
	Glu	Ser	Asn	Phe	Thr	Leu	Val	Gly	Asp	Asp	Gly	Thr	Asn	Lys	Glu	Ala	
35						180				185					190		

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	tgg tgt tct ggc cga gtg tgc tgt gag ggc atg ctt atc cag ctg agg	790
5	Trp Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg	
	210 215 220	
	ttc ctc aag aga caa gac tta ctg aat gtc ctg gcc cgg atg atg agg	838
	Phe Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg	
	225 230 235	
10	cca gtg agt gat caa gtg caa ata aaa gta acc atg aat gat gaa gac	886
	Pro Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp	
	240 245 250 255	
	atg gat acc tac gta ttt gct gtt ggc aca cgg aaa gcc ttg gtg cga	934
	Met Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg	
15	260 265 270	
	cta cag aaa gag atg cag gat ttg agt gag ttt tgt agt gat aaa cct	982
	Leu Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro	
	275 280 285	
	aag tct gga gca aag tat gga ctg ccg gac tct ttg gcc atc ctg tca	1030
20	Lys Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser	
	290 295 300	
	gag atg gga gaa gtc aca gac gga atg atg gat aca aag atg gtt cac	1078
	Glu Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His	
	305 310 315	
25	ttt ctt aca cac tat gct gac aag att gaa tct gtt cat ttt tca gac	1126
	Phe Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp	
	320 325 330 335	
	cag ttc tct ggt cca aaa att atg caa gag gaa ggt cag cct tta aag	1174
	Gln Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys	
30	340 345 350	
	cta cct gac act aag agg aca ctg ttg ttt aca ttt aat gtg cct ggc	1222
	Leu Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly	
	355 360 365	
	tca ggt aac act tac cca aag gat atg gag gca ctg cta ccc ctg atg	1270
35	Ser Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met	

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	370	375	380	
	aac atg gtg att tat tct att gat aaa gcc aaa aag ttc cga ctc aac	1318		
	Asn Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn			
	385	390	395	
5	aga gaa ggc aaa caa aaa gca gat aag aac cgt gcc cga gta gaa gag	1366		
	Arg Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu			
	400	405	410	415
	aac ttc ttg aaa ctg aca cat gtg caa aga cag gaa gca gca cag tct	1414		
	Asn Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser			
10	420	425	430	
	cgg cgg gag gag aaa aaa aga gca gag aag gag cga atc atg aat gag	1462		
	Arg Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu			
	435	440	445	
	gaa gat cct gag aaa cag cgc agg ctg gag gag gct gca ttg agg cgt	1510		
15	Glu Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg			
	450	455	460	
	gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa caa atc aaa	1558		
	Glu Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys			
	465	470	475	
20	gtg aaa gcc atg taaagccatc ccagagattt gagttctgat gccacctgta	1610		
	Val Lys Ala Met			
	480			
	agctctgaat tcacaggaaa catgaaaaac gccagtcctat ttctcaacct taaatttcag	1670		
	acagtccttg gcaactgaga aatccttatt tcacatccta ctctgttttg gggttggggg	1730		
25	tttacagaga ttgaagatac ctggaaaagg ctctgtttca agaatttttt ttccagata	1790		
	atcaaattat ttgtattatt ttataaaaagg aatgatctat gaaatctgtg taggttttaa	1850		
	atattttaaa aattataata caaatcatca gtgcttttag tacttcagtg tttaaagaaa	1910		
	taccatgaaa tttataggta gataaccaga ttgttgcttt ttgtttaaac caagcagttg	1970		
	aaatggctat aaagactgac tctaaaccaa gattctgcaa ataatgattg gaattgcaca	2030		
30	ataaacattg cttgatgttt	2050		
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35	<213> Homo sapiens			

160/177

<220>

<221> CDS

<222> (70)...(1074)

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 Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg
 1 5 10

10 agg ctg cag aca ctt gct gtc cta cag ttt gtc ttc tcc ttc ttg gca 156
 Arg Leu Gln Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala
 15 20 25
 ctg gcc gag atc tgc act gtg ggc ttc ata gcc ctc ctg ttt aca aga 204
 Leu Ala Glu Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg

15 30 35 40 45
 ttc tgg ctc ctc act gtc ctg tat gcg gcc tgg tgg tat ctg gac cga 252
 Phe Trp Leu Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg
 50 55 60
 gac aag cca cgg cag ggg ggc cgg cac atc cag gcc atc agg tgc tgg 300
 Asp Lys Pro Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp

20 65 70 75
 act ata tgg aag tac atg aag gac tat ttc ccc atc tcg ctg gtc aag 348
 Thr Ile Trp Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys
 80 85 90

25 act gct gag ctg gac ccc tct cgg aac tac att gcg ggc ttc cac ccc 396
 Thr Ala Glu Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro
 95 100 105
 cat gga gtc ctg gca gtc gga gcc ttt gcc aac ctg tgc act gag agc 444
 His Gly Val Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser

30 110 115 120 125
 aca ggc ttc tct tcg atc ttc ccc ggt atc cgc ccc cat ctg atg atg 492
 Thr Gly Phe Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met
 130 135 140
 ctg acc ttg tgg ttc cgg gcc ccc ttc ttc aga gat tac atc atg tct 540

35 Leu Thr Leu Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser

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	145	150	155	
	gca ggg ttg gtc aca tca gaa aag gag agt gct gct cac att ctg aac	588		
	Ala Gly Leu Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn			
	160	165	170	
5	agg aag ggt ggc gga aac ttg ctg ggc atc att gta ggg ggt gcc cag	636		
	Arg Lys Gly Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln			
	175	180	185	
	gag gcc ctg gat gcc agg cct gga tcc ttc acg ctg tta ctg cgg aac	684		
	Glu Ala Leu Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn			
10	190	195	200	205
	cga aag ggc ttc gtc agg ctc gcc ctg aca cac ggg gca ccc ctg gtg	732		
	Arg Lys Gly Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val			
	210	215	220	
	cca atc ttc tcc ttc ggg gag aat gac cta ttt gac cag att ccc aac	780		
15	Pro Ile Phe Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn			
	225	230	235	
	tct tct ggc tcc tgg tta cgc tat atc cag aat cgg ttg cag aag atc	828		
	Ser Ser Gly Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile			
	240	245	250	
20	atg ggc atc tcc ctc cca ctc ttt cat gcc cgt ggt gtc ttc cag tac	876		
	Met Gly Ile Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr			
	255	260	265	
	agc ttt ggt tta ata ccc tac cgc cgg ccc atc acc act gtg gtg ggg	924		
	Ser Phe Gly Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly			
25	270	275	280	285
	aag ccc atc gag gta cag aag acg ctg cat ccc tcg gag gag gag gtg	972		
	Lys Pro Ile Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val			
	290	295	300	
	aac cag ctg cac cag cgt tat atc aaa gag ctg tgc aac ctc ttc gag	1020		
30	Asn Gln Leu His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu			
	305	310	315	
	gcc cac aaa ctt aag ttc aac atc cct gct gac cag cac ttg gag ttc	1068		
	Ala His Lys Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe			
	320	325	330	
35	tgc tgagcccaa agggcagggc caacattagg gagccagca ggaggtgctg	1120		

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Cys

5 tgctgagaag acctcctgga ggtgtttgtt gaacatatct gcagagcctt cccagactcc 1180
 tgcaaatcca acccatatca ggctgtaagt cagagcaggc aatgcagaag aggagaccag 1240
 accaagggggt cagctggggc taggacagtg agggctgcta gaggggctgg gcctctcttt 1300
 5 gcacatggac actgggccc cctctatatt gagtggctctg ttaacattca ttggtggctg 1360
 attccaaaag atgagagcca aagctgcacg gactcgagtc ctaggctgca cactcaca 1420
 gcctctcttc tactgcattc tgttggtcga agcaagtcac aaccagcag attcaaggag 1480
 taagggaatag gatcccccctc tggatgggag gagcagcaat gtcattattac aaaagggtgt 1540
 ggacacatgc agggattctt actgccgtct ttgcaacaa tccaccaaaa cttaaaaact 1600
 10 aaaagcctga agcacazyca ctctccccc caggcacaca caccctggaa ttccctgtgt 1660
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 atctccctct cgtctctccc tgttgatccc tcatgcacag ccacagcgag ctgtctaaaa 1780
 cacaaagctg accgcgccat ttctactca gcctcctcc atgacctcc attgtccta 1840
 ggatagggtt tggaccagtc tgaatccaga ggatcaggat ccagcaggaa ccaggagata 1900
 15 atttgaggag ggtttaaaaa ggaaccattt tttgaggtgt gtgactgtt tccacctga 1960
 ggcttggaag gatgaatgga agcagcagtt cctgaaccag gaagactcat gtgtgggggc 2020
 cattgttgtt caaggggcac gaacaggtct ggtgacctg caaggaggga gccaggagca 2080
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 caactagaag ctggaggga ggagggcctg tggtgcagt ccaggcatgt aggcctcctg 2200
 20 ggaaaggag aatggcaag acaggcagag tggatctgga ggggtcaacg gaagacggaa 2260
 catgtccact tccaggccc agcttctcag cctgccgttt gccactctcc agcatctggc 2320
 ccagcctgct cactctcctc tctctctc cctactccg tctccctc actcggaacc 2380
 atttgcattt ctttgtctca gctatattgt ctccctctg agtttttgcc catgatgtg 2440
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 25 atctacaat actgatttta tctgtgaaa gaagtcttc ccagtgcctc tggttgacag 2560
 ggggttctc tggcttctc agactttctg ttctccacc acagccctta gcacctggg 2620
 gaggaggtgt tctgtccag gtaaatgctg cgcgaatgcc cctgcctcta gtgcactcc 2680
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<210> 143

<211> 1136

<212> DNA

<213> Homo sapiens

35

<220>

163/177

<221> CDS

<222> (32)...(835)

<400> 143

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	1 5	
	agc cct ggg gtc ctg gtg cgg acc ggg cac acc gtg ctg acc tgg gga	100
	Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly	
10	10 15 20	
	atc acg ctg gtg ctc ttc ctg cac gat acc gag ctg cgg caa tgg gag	148
	Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Gln Trp Glu	
	25 30 35	
	gag cag ggg gag ctg ctc ctg ccc ctc acc ttc ctg ctc ctg gtg ctg	196
15	Glu Gln Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Val Leu	
	40 45 50 55	
	ggc tcc ctg ctg ctc tac ctc gct gtg tca ctc atg gac cct ggc tac	244
	Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr	
	60 65 70	
20	gtg aat gtg cag ccc cag cct cag gag gag ctc aac gag gag cag aca	292
	Val Asn Val Gln Pro Gln Pro Gln Glu Glu Leu Lys Glu Glu Gln Thr	
	75 80 85	
	gcc atg gtt cct cca gcc atc cct ctt cgg cgc tgc aga tac tgc ctg	340
	Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu	
25	90 95 100	
	gtg ctg cag ccc ctg agg gct cgg cac tgc cgt gag tgc cgc cgt tgc	388
	Val Leu Gln Pro Leu Arg Ala Arg His Cys Arg Glu Cys Arg Arg Cys	
	105 110 115	
	gtc cgc cgc tac gac cac cac tgc ccc tgg atg gag aac tgt gtg gga	436
30	Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly	
	120 125 130 135	
	gag cgc aac cac cca ctc ttt gtg gtc tac ctg gcg ctg cag ctg gtg	484
	Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Gln Leu Val	
	140 145 150	
35	gtg ctt ctg tgg ggc ctg tac ctg gca tgg tca ggc ctc cgg ttc ttc	532

	Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe Phe	
	155 160 165	
	cag ccc tgg ggt ctg tgg ttg cgg tcc agc ggg ctc ctg ttc gcc acc	580
	Gln Pro Trp Gly Leu Trp Leu Arg Ser Ser Gly Leu Leu Phe Ala Thr	
5	170 175 180	
	ttc ctg ctg ctg tcc ctc ttc tgg ttg gtg gcc agc ctg ctc ctc gtc	628
	Phe Leu Leu Leu Ser Leu Phe Ser Leu Val Ala Ser Leu Leu Leu Val	
	185 190 195	
	tgg cac ctc tac ctg gtg gcc agc aac acc acc acc tgg gaa ttc atc	676
10	Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Thr Trp Glu Phe Ile	
	200 205 210 215	
	tcc tca cac cgc atc gcc tat ctc cgc cag cgc ccc agc aac ccc ttc	724
	Ser Ser His Arg Ile Ala Tyr Leu Arg Gln Arg Pro Ser Asn Pro Phe	
	220 225 230	
15	gac cga ggc ctg acc cgc aac ctg gcc cac ttc ttc tgt gga tgg ccc	772
	Asp Arg Gly Leu Thr Arg Asn Leu Ala His Phe Phe Cys Gly Trp Pro	
	235 240 245	
	tca ggg tcc tgg gag acc ctc tgg gct gag gag gag gaa gag ggc agc	820
	Ser Gly Ser Trp Glu Thr Leu Trp Ala Glu Glu Glu Glu Glu Gly Ser	
20	250 255 260	
	agc cca gct gtt taggggtgct ggaggccggg ctacogtett gtgcetga	870
	Ser Pro Ala Val	
	265	
	aaaccacggg gccctgtccc agctgggggtg agcgcctcaga gggccctgggg ccctcactcc	930
25	tgccacgcgc tcccagacc cagaacggag cttcaagtca gacagatccc tgccttggtg	990
	ggcagttctg ccttccaagg aagaaggga agaaaaggac ctgtgggtgg ctcaggccca	1050
	agcagacccc gggtccacc ccagcccccgc ccaggctgct gccagtgcac acctttacaa	1110
	atttaatatata aagcaagtc agtett	1136
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	<212> DNA	
	<213> Homo sapience	
	<220>	
35	<221> CDS	

165/177

<222> (13)...(333)

<400> 144

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	1 5 10	
	aac aaa gtg ctg agg tac aag ccc ccg ccg agc gaa tgt aac ccg gcc	96
	Asn Lys Val Leu Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala	
	15 20 25	
10	ttg gac gac ccg acg ccg gac tac atg aac ctg ctg ggc atg atc ttc	144
	Leu Asp Asp Pro Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe	
	30 35 40	
	agc atg tgc ggc ctc atg ctt aag ctg aag tgg tgt gct tgg gtc gct	192
	Ser Met Cys Gly Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala	
15	45 50 55 60	
	gtc tac tgc tcc ttc atc agc ttt gcc aac tct cgg agc tcg gag gac	240
	Val Tyr Cys Ser Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp	
	65 70 75	
	acg aag caa atg atg agt agc ttc atg ctg tcc atc tct gcc gtg gtg	288
20	Thr Lys Gln Met Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val	
	80 85 90	
	atg tcc tat ctg cag aat cct cag ccc atg acg ccc cca tgg	340
	Met Ser Tyr Leu Gln Asn Pro Gln Pro Met Thr Pro Pro Trp	
	95 100 105	
25	tgataccagc ctagaagggt cacattttgg accctgtcta tccactaggc ctgggctttg	390
	gctgctaaac ctgctgcctt cagctgccat cctggacttc cctgaatgag gccgtctcgg	450
	tgcctccagc tggatagagg gaacctggcc ctttcctagg gaacacccta ggcctaccoc	510
	tctgctctcc ctccctctgc ctgctgetgg gggagatget gtccatgttt ctagggggat	570
	tcatttgctt tctcgttgaa acctgttgtt aataaagttt ttcactcag	619
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<210> 145

<211> 864

<212> DNA

<213> Homo sapience

35 <220>

166/177

<221> CDS

<222> (111)...(785)

<400> 145

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	gagacgccgc ctccgatcc ccgcgcgggc gggaccgggc ggccggcacc atg acc	116
	Met Thr	
	1	
10	ctg ttt cac ttc ggg aac tgc ttc gct ctt gcc tac ttc ccc tac ttc	164
	Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro Tyr Phe	
	5 10 15	
	atc acc tac aag tgc agc ggc ctg tcc gag tac aac gcc ttc tgg aaa	212
	Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe Trp Lys	
	20 25 30	
15	tgc gtc cag gct gga gtc acc tac ctc ttt gtc caa ctc tgc aag atg	260
	Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys Lys Met	
	35 40 45 50	
	ctg ttc ttg gcc act ttc ttt ccc acc tgg gaa ggc ggc atc tat gac	308
	Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile Tyr Asp	
20	55 60 65	
	ttc att ggg gag ttc atg aag gcc agc gtg gat gtg gca gac ctg ata	356
	Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp Leu Ile	
	70 75 80	
	ggc cta aac ctt gtc atg tcc cgg aat gcc ggc aag gga gag tac aag	404
25	Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu Tyr Lys	
	85 90 95	
	atc atg gtt gct gcc ctg ggc tgg gcc act gct gag ctt att atg tcc	452
	Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile Met Ser	
	100 105 110	
30	ogc tgc att ccc cta tgg gtc gga gcc cgg ggc att gag ttt gac tgg	500
	Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe Asp Trp	
	115 120 125 130	
	aag tac atc cag atg agc ata gac tcc aac atc agt ctg gtc cat tac	548
	Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val His Tyr	
35	135 140 145	

167/177

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atc gtc gcg tct gct cag gtc tgg atg ata aca cgc tat gat ctg tac      596
Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr
      150      155      160
cac acc ttc cgg cca gct gtc ctc ctg ctg atg ttc ctc agt gtc tac      644
5 His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr
      165      170      175
aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc tcg ctg gcc agt      692
Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser
      180      185      190
10 tgg gca gct cta ctg gcc cga gca gtg gta acg ggg ctg ctg gcc ctc      740
Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu
      195      200      205      210
agc act ttg gcc ctg tat gtc gcc gtt gtc aat gtg cac tcc taggcttg      790
Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser
      215      220
15 gtgtctcaga cattgatgta ccttttccct gctcgcctcc aggttttagt gaagtaaaca      850
gtatttgaa agtt      864

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20 <211> 1527
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25 <222> (25)...(801)

<400> 146
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30      1      5
ctc gtg tat tcg gtg ccg cga ctt tca cga tgg ctc gcc caa cct tac      99
Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr
      10      15      20      25
tac ctt ctg tcg gcc ctg ctc tct gct gcc ttc cta ctc gtg agg aaa      147
35 Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

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168/177

			30				35				40																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																					</
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Asn Leu Asn Glu Leu Tyr Gln Arg Ala Lys Lys Leu Ser Lys Ala Gly
 220 225 230
 gac aat atc cct gag gag cag cct gtg gct tca acc ccc acc aca gtg 771
 Asp Asn Ile Pro Glu Glu Gln Pro Val Ala Ser Thr Pro Thr Thr Val
 5 235 240 245
 tca gat ggg gaa aac aag aag gat aaa taagatcctc ac 810
 Ser Asp Gly Glu Asn Lys Lys Asp Lys
 250 255
 tttggcagtg ctccctctcc tgtcaattcc aggcctctttc cataaccaca agcctgagge 870
 10 tgcagccttt tatttatgtt ttcccttttg ctgtgactgg gtggggcagc atgcagcttc 930
 tgattttaaa gaggcctcct ggaattgtc aggcacccta caggaaaggcc tgccatgctg 990
 tggccaaactg ttctactgga gcaagaaaga gatctcatag gacggagggg gaaatggttt 1050
 cctccaagc ttgggtcagt gtgttaactg cttatcagct attcagacat ctccatggtt 1110
 tctccatgaa actctgtggt ttcatcattc cttcttagtt gacctgcaca gcttggttag 1170
 15 acctagattt aaccctaagg taagatgctg ggtatagaa cgctaagaat tttcccccac 1230
 ggactcttgc ttccttaagc cctcttggtc tegtattatg tcttcattaa aagtataagc 1290
 ctaactttgt cgctagtctt aaggagaaac ctttaaccac aaagttttta tcattgaaga 1350
 caatattgaa caaccacctc ttttgtggg attgagaagg ggtgaataga ggcttgagac 1410
 tttcctttgt gtggtaggac ttggaggaga aatccctctg actttcacta accctctgac 1470
 20 atactcccca caccagttg atggctttcc gtaataaaaa gattgggatt tcctttt 1527

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 aagtagtgtg tccggcgcgc tgttccagct ccgcgttgtt ccgcgagaaa gcgagaggcc 120
 gagcccgggc tgggtgcg atg gcc gcg gtg gtg gcc aag cgg gaa ggg ccg 170
 Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro
 35 1 5 10

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ccg ttc atc agc gag gcg gcc gtg cgg ggc aac gcc gcc gtc ctg gat      218
Pro Phe Ile Ser Glu Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp
           15                20                25
tat tgc cgg acc tcg gtg tca gcg ctg tcg ggg gcc acg gcc ggc atc      266
5  Tyr Cys Arg Thr Ser Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile
           30                35                40
ctc ggc ctc acc ggc ctc tac gcc ttc atc ttc tac ctg ctc gcc tcc      314
Leu Gly Leu Thr Gly Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser
           45                50                55
10 gtc ctg ctc tcc ctg ctc ctc att ctc aag gcg gga agg agg tgg aac      362
Val Leu Leu Ser Leu Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn
           60                65                70                75
aaa tat ttc aaa tca cgg aga cct ctc ttt aca gga ggc ctc atc ggg      410
Lys Tyr Phe Lys Ser Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly
15 ggc ctc ttc acc tac gtc ctg ttc tgg acg ttc ctc tac gcc atg gtg      458
Gly Leu Phe Thr Tyr Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val
           95                100                105
20 cac gtc tac tgaatgggg gcccgggga cttttttaa aaa                      500
His Val Tyr
           110
ccagatcggg aggactgtgg ccagcaatta acaccatgta gaattcetta gttottaagt      560
ggttgaattc gctgcttgtt ctgtaacgtt ataaataatt tatatctgaa gacggagagc      620
ctgtaatatt cttcagatta aatgaagcgt gagacactt                          659
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ggacaag atg gtt tac atc tcg aac gga caa gtg ttg gac agc cgg agt      109
      Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser
              1              5              10
cag tct cca tgg aga tta tct ttg ata aca gat ttc ttc tgg gga ata      157
5  Gln Ser Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile
      15              20              25              30
gct gag ttt gtg gtt ttg ttt ttc aaa act ctg ctt cag caa gat gtg      205
Ala Glu Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val
              35              40              45
10 aaa aaa aga aga agc tat gga aac tca tct gat tcc aga tat gat gat      253
Lys Lys Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp
              50              55              60
gga aga ggg cca cca gga aac cct ccc cga aga atg ggt aga atc aat      301
Gly Arg Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn
15      65              70              75
cat ctg cgt ggc cct agt ccc cct cca atg gct ggt gga tgaggaaggt      350
His Leu Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly
              80              85              90
20 aaatgtctgc tctaagaagc agacaaccgg acatgcgcac tcatagcaga aggaaccat      410
caagaagtgg aaggetgacc atgatgagca gtagatgaat gtgtatgtct aaacaaggac      470
tgctctgtgt cctcacagat gaatgaggtc atgctgggaa ttcctctctgc agggaaactgg      530
cctgactgac atgcagtccc ataaatgcag atgtttgtct cattaccttt ttgtatagtt      590
tattaaagta ttaatatagt ttaataaagt aaatatTTTT aggttgacaga atggactcct      650
catctttata ttcacgaaaa agcaatctga agaaaacaaa taaaagocctg tgtatttagc      710
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	Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser	
	1 5 10 15	
	aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc gcc ctc	151
5	Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu	
	20 25 30	
	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctt cac gca gtc	199
	Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val	
	35 40 45	
10	aag aac gac ttc cag att tgg agg ttg ata tgt gga aga ata att tgc	247
	Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys	
	50 55 60	
	ctt gat ttg aaa gat act ttc tgc agt agt ctg ctt att tat aat ttt	295
	Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe	
15	65 70 75 80	
	agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca tcc ttt ttg	343
	Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu	
	85 90 95	
	ctg ggt tcc tgg gtt ttg tca gcc tta ttt gac ttt ctc ctc att gaa	391
20	Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu	
	100 105 110	
	gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg cct tct	439
	Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser	
	115 120 125	
25	gga ttc ctg gca cct g-g ttt gct ctg ttt gta cca ttt tac tgc tcc	487
	Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser	
	130 135 140	
	ata cca aga gtc caa gtg gca caa att ctg ggt ccg ttg tcc atc aca	535
	Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr	
30	145 150 155 160	
	aac aag aca ttg att tat ata ttg gga ctg cag ctt ttc acc tct ggt	583
	Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly	
	165 170 175	
	tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc	631
35	Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys	

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	180	185	190	
	tac gac agc aaa atg ttc cag gtg cat cag gtg ctc tgc atc ccc agc			679
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser			
	195	200	205	
5	tgg atg gca aaa ttc ttt tct tgg aca ctt gaa ccc atc ttc tct tct			727
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser			
	210	215	220	
	tca gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac			775
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp			
10	225	230	235	240
	atc cag aga cag cag aga atg gag ctg ctg gac cgg cag ctg atg ttc			823
	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe			
	245	250	255	
15	tct cag ttt gca caa ggg agg cga cag aga cag cag cag gga gga atg			871
	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met			
	260	265	270	
	atc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta			919
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val			
	275	280	285	
20	aac tat cag ggc ggt cgg cag tct gag cca gca gcg ccc cct cta gaa			967
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu			
	290	295	300	
	gtt tct gag gaa cag gtc gcc cgg ctc atg gag atg gga ttt tcc aga			1015
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg			
25	305	310	315	320
	ggc gat gct ttg gaa gcc ctg aga gct tca aac aat gac ctc aat gtc			1063
	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val			
	325	330	335	
	gcc acc aac ttc ctg ctg cag cac tgcagtcacc aggcacacac tgg			1110
30	Ala Thr Asn Phe Leu Leu Gln His			
	340			
	gaccggaccg gcagccgagt gacagtgcgt ggtccccacc atcagatcag cccggggacc			1170
	gagcatctct ggtgctgatg ttcttggtggg aagagggagg ttccaccgca cccctgcct			1230
	caaccgcaag actgttgccg ttttagtggt gagataagtt tgccattaca ttagcatgta			1290
35	ttttctatct atatttttta ttgggcattt tccctaggtt ggagagtcag cactcgtttt			1350

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	gaatggtttt aaatgcatt aaatggaag atttctgcag gcagttgaat ggcactccag	1410
	atggggaatt gctgtaaccc tcttactgta acatgtcacc tctgcgtcg tgatggggag	1470
	agggtaattg tacttcacaa aggacatgac agatccttct tcatggactt ttttagttac	1530
	tgttttttct ctcaacttg ttttcgaatc tctggggagt gaggagagaa caggagctg	1590
5	aatcctcccc caagctgttc caggccagag gactctgcag taccctctcc tacatctagt	1650
	aacaaagaat ggtgataacc atgcactggt tcaaggttct ggagttctcc atgaaactg	1710
	ggttaatttt gctcagagta tccggagtta gccactaggc tgcgggtgaa atgggatgga	1770
	gtagaacaac agcaggettcc ctggagccac atgggctgac tagggcactc tgtggctggc	1830
	ctggcacggg ctacagccag gaagaggaga aacgatccct tgcctgcccc tccctgtggc	1890
10	agggctaact gctgggacct cctggctcgc agccagccag cccctggca gcaggtctc	1950
	ctcagggctt gggctctcaa cctgtggcga caggaggcag ggcagactgt ggaggacag	2010
	atgcaggta gggagaggga aggcagggtt ggaccgccat gagcatgaaa agaccggaag	2070
	caagttgact cttgcaatgt gcaactgtta tgttctgcaa aatgagcaac gatgtatcaa	2130
	attgatgcaa atttagatgt tgatacttac aataaagttt ttaatgtgtt tt	2182
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	acgtgcctcc tggctccgac gtatctgcaa gctccccagt ctactccat tcttcccca	120
	cctggcgcgc acctgctcaa gaccagggtc ctgccagcag ctaggagggc gcgtgccagg	180
	ggcgctaggg aactgcggag cgcgcgcgcc atg ggg ccg ccg cct ggg gcc	231
	Met Gly Pro Pro Pro Gly Ala	
30	1 5	
	ggg gtc tcc tgc cgc ggt ggc tgc ggc ttt tcc aga ttg ctg gca tgg	279
	Gly Val Ser Cys Arg Gly Gly Cys Gly Phe Ser Arg Leu Leu Ala Trp	
	10 15 20	
	tgc ttc ctg ctg gcc ctg agt ccg cag gca ccc ggt tcc cgg ggg gct	327
35	Cys Phe Leu Leu Ala Leu Ser Pro Gln Ala Pro Gly Ser Arg Gly Ala	

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	25	30	35	
	gaa gca gtg tgg acc gcg tac ctc aac gtg tcc tgg cgg gtt ccg cac			375
	Glu Ala Val Trp Thr Ala Tyr Leu Asn Val Ser Trp Arg Val Pro His			
	40	45	50	55
5	acg gga gtg aac cgt acg gtg tgg gag ctg agc gag gag ggc gtg tac			423
	Thr Gly Val Asn Arg Thr Val Trp Glu Leu Ser Glu Glu Gly Val Tyr			
	60	65	70	
	ggc cag gac tgg ccg ctg gag cct gtg gct ggg gtc ctg gta ccg ccc			471
	Gly Gln Asp Ser Pro Leu Glu Pro Val Ala Gly Val Leu Val Pro Pro			
10	75	80	85	
	gac ggg ccc ggg gcg ctt aac gcc tgt aac ccg cac acg aat ttc acg			519
	Asp Gly Pro Gly Ala Leu Asn Ala Cys Asn Pro His Thr Asn Phe Thr			
	90	95	100	
	gtg ccc acg gtt tgg gga agc acc gtg caa gtc tct tgg ttg gcc ctc			567
15	Val Pro Thr Val Trp Gly Ser Thr Val Gln Val Ser Trp Leu Ala Leu			
	105	110	115	
	atc caa cgc gcc ggg gcc tgc acc ttc gca gac aag atc cat ctg gct			615
	Ile Gln Arg Gly Gly Gly Cys Thr Phe Ala Asp Lys Ile His Leu Ala			
	120	125	130	135
20	tat gag aga ggg gcg tct gga gcc gtc atc ttt aac ttc ccc ggg acc			663
	Tyr Glu Arg Gly Ala Ser Gly Ala Val Ile Phe Asn Phe Pro Gly Thr			
	140	145	150	
	cgc aat gag gtc atc ccc atg tct cac ccg ggt gca gta gac att gtt			711
	Arg Asn Glu Val Ile Pro Met Ser His Pro Gly Ala Val Asp Ile Val			
25	155	160	165	
	gca atc atg atc gcc aat ctg aaa gcc aca aaa att ctg caa tct att			759
	Ala Ile Met Ile Gly Asn Leu Lys Gly Thr Lys Ile Leu Gln Ser Ile			
	170	175	180	
	caa aga gcc ata caa gtg aca atg gtc ata gaa gta ggg aaa aaa cat			807
30	Gln Arg Gly Ile Gln Val Thr Met Val Ile Glu Val Gly Lys Lys His			
	185	190	195	
	ggc cct tgg gtg aat cac tat tca att ttt ttc gtt cct gtg tcc ttt			855
	Gly Pro Trp Val Asn His Tyr Ser Ile Phe Phe Val Ser Val Ser Phe			
	200	205	210	215
35	ttt att att acg gcg gca act gtg gcc tat ttt atc ttt tat tct gct			903

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	Phe Ile Ile Thr Ala Ala Thr Val Gly Tyr Phe Ile Phe Tyr Ser Ala	
	220 225 230	
	cga agg cta cgg aat gca aga gct caa agc agg aag cag agg caa tta	951
	Arg Arg Leu Arg Arg Asn Ala Arg Ala Gln Ser Arg Lys Gln Arg Gln Leu	
5	235 240 245	
	aag gca gat gct aaa aaa gct att gga agg ctt caa cta cgc aca ctg	999
	Lys Ala Asp Ala Lys Lys Ala Ile Gly Arg Leu Gln Leu Arg Thr Leu	
	250 255 260	
	aaa caa gga gac aag gaa att ggc cct gat gga gat agt tgt gct gtg	1047
10	Lys Gln Gly Asp Lys Glu Ile Gly Pro Asp Gly Asp Ser Cys Ala Val	
	265 270 275	
	tgc att gaa ttg tat aaa cca aat gat ttg gta cgc atc tta acg tgc	1095
	Cys Ile Glu Leu Tyr Lys Pro Asn Asp Leu Val Arg Ile Leu Thr Cys	
	280 285 290 295	
15	aac cat att ttc cat aag aca tgt gtt gac cca tgg ctg tta gaa cac	1143
	Asn His Ile Phe His Lys Thr Cys Val Asp Pro Trp Leu Leu Glu His	
	300 305 310	
	agg act tgc ccc atg tgc aaa tgt gac ata ctc aaa gct ttg gga att	1191
	Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile	
20	315 320 325	
	gag gtg gat gtt gaa gat gga tca gtg tct tta caa gtc cct gta tcc	1239
	Glu Val Asp Val Glu Asp Gly Ser Val Ser Leu Gln Val Pro Val Ser	
	330 335 340	
	aat gaa ata tct aat agt gcc tcc tcc cat gaa gag gat aat cgc agc	1287
25	Asn Glu Ile Ser Asn Ser Ala Ser Ser His Glu Glu Asp Asn Arg Ser	
	345 350 355	
	gag acc gca tca tct gga tat gct tca gta cag gga aca gat gaa ccg	1335
	Glu Thr Ala Ser Ser Gly Tyr Ala Ser Val Gln Gly Thr Asp Glu Pro	
	360 365 370 375	
30	cct ctg gag gaa cac gtg cag tca aca aat gaa agt cta cag ctg gta	1383
	Pro Leu Glu Glu His Val Gln Ser Thr Asn Glu Ser Leu Gln Leu Val	
	380 385 390	
	aac cat gaa gca aat tct gtg gca gtg gat gtt att cct cat gtt gac	1431
	Asn His Glu Ala Asn Ser Val Ala Val Asp Val Ile Pro His Val Asp	
35	395 400 405	

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aac cca acc ttt gaa gaa gac gaa act cct aat caa gag act gct gtt 1479
Asn Pro Thr Phe Glu Glu Asp Glu Thr Pro Asn Gln Glu Thr Ala Val
410 415 420
cga gaa att aaa tct taaaatctgt gtaaatagaa aacttgaacc attagt 1530
5 Arg Glu Ile Lys Ser
425
aataacagaa ctgccaatca gggcctagtt tctattaata aattggataa atttaataaa 1590
ataagagtga tactgaaagt gtcagatga ctaatatattat gctatagtta aatggottaa 1650
aatatttaac ctgttaactt ttttcacaaa actcattata atatttttca taggcaagtt 1710
10 tccctcagtt agtgataaca acatttttag acattcaaaa ctgtcttcaa gaagtcacgt 1770
ttttcattta taacaatttt cttataaaaa catgttgott ttaaaatgtg gagtagctgt 1830
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atgtgtcagg gtttttctcc aggtgcttat attgatctgg aattgtaatg taaaaagcaa 1950
tgcaaaactta ggcgagtact tcttgaaatg tctatttaag ctgctttaag ttaatagaaa 2010
15 agattaaagc aaaatattca tttttacttt ttcttatttt taaaattagg ctgaatgtac 2070
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agtgcacatca acttgacaca agattagaca aaaaattcct tacaanaata ctgtgtaact 2190
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attgctaag acagagtaag taacactaat attggtcatt gatcttcggt catgaattag 2310
20 tctacagaaa aaaaatgttc tgtaaaatta gtctgttgaa aatgttttcc aaacaatgtt 2370
actttgaaaa ttgagtttat gtttgacctt aatgggctaa aattatatta gataaactaa 2430
aattctgtcc gtgtaactat aaattttgtg aatgcatttt cctggtgttt gaaaaagaag 2490
ggggggagaa ttccaggtgc cttaatataa agtttgaaac ttcacccacc aaagttaaat 2550
agagctattt aaaaatgcac tttatttgta ctctgtgagg cttttgtttt agaattttgt 2610
25 tcaaattata gcagaattta ggcaaaaata aaacagacat gtatttttgt ttgctgaatg 2670
gatgaaccac ttgcattctt gtacactgat ttgaaatgct gtaaatatgt cccaatttgt 2730
attgattctc tttaaatata aaatgtaaat aaaatattcc aat 2773